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IS THERE A COMMON DENOMINATOR IN SCLERODERMA, DERMATOMYOSITIS, DISSEMINATED LUPUS ERYTHEMATOSUS, THE LIBMAN-SACKS SYNDROME AND POLYARTERITIS NODOSA?*

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SCLERODERMA, dermatomyositis, disseminated lupus erythematosus, the Libman-Sacks syndrome and polyarteritis nodosa constitute a group of diseases of unknown etiology that are apparently unrelated in their presenting clinical features. The widespread visceral involvement in each is obscured by certain dominating focal manifestations, which serve as the clinical basis for the differentiation of these syndromes from each other. Striking similarities, however, in the detailed pathology of these various conditions require evaluation for a possible relation or common denominator among them. This communication reports a case of scleroderma that presented visceral features common to other diseases in this group. The systemic symptoms and pathology of these syndromes are discussed to define their differences and to determine whether any common relation exists.

CASE REPORT

A 51-year-old unmarried secretary was first admitted to the hospital for study on August 23, 1939, because of generalized pigmentation suggestive of Addison's disease. The present illness first became manifest in the fall of 1937, when she noted that on awaking in the morning there was marked numbness and coldness of both hands, especially the right. In the winter of 1937–1938, both hands on exposure to cold became painful and showed whitish-blue discoloration. There was never any pain or numbness of the feet. In January, 1938, a diagnosis of arthritis was made, and x-ray films of the hands were interpreted as showing arthritic changes. The patient lost 18 pounds on a reducing diet, and received two series of vaccine injections, each lasting approximately 3 months. She consulted another physician in the spring of 1939 because of persistent severe pain in the right hand, hardness of the finger tips bilaterally and difficulty in typing. He doubted the diagnosis of arthritis, and believed that the patient had scleroderma. Because of a basal metabolic rate of −27 per cent, the patient was given between 2 and 3 gr. of thyroid daily, which she took regularly to the date of admission. She also received Brewer's yeast, belladonna and phenobarbital. Her finger tips became much softer, and she could type without difficulty. During the summer of 1939, her right wrist became very stiff and painful, and the fingers gradually contracted and became so stiff that she could not close her fist tightly. The patient had noticed that her skin darkened rapidly every summer, but that throughout the last year her chest had remained tanned. During that winter the skin continued to darken and became very shiny. Her appetite and strength remained fairly good, and her weight before admission was 128 pounds. Two weeks before admission, she developed a slightly sore area at the base of the 5th metatarsal bone of the left foot, which a week later became infected and discharged pus.

The past history was not remarkable. The patient had always been in excellent health. She had typhoid fever 27 years before admission, and a hysterectomy for fibroid uterus 19 years later. There was no history of scarlet fever or rheumatic fever. The system and family histories were noncontributory. She had used no tobacco or alcohol.

Physical examination revealed intensely tanned skin, the backs of the hands being almost negroid in appearance. The skin of the anterior chest was glistening brown and stretched very tightly over the underlying structures. The skin over the malar portion of the face was likewise very taut. On the backs of the hands, palms and fingers, the skin and subcutaneous tissues were thick and brawny. In the mouth there appeared one small area that was suggestive of pigmentation. Hyperkeratotic plaques were abundant on the abdomen. The fundi and the thyroid gland were normal. The heart and lungs showed no abnormalities; the blood pressure was 114/74. Abdominal examination revealed no unusual findings, and the peripheral reflexes were equal and hyperactive. The fingers were tapering and cold, and neither hand could close completely. The right wrist was extremely painful to palpation and movement. The skin over the legs was normal in texture except for moderate brawny edema of the left leg, with slight pitting at the ankle. At the base of the 5th metatarsal on the left, there was a fairly well-healed infection. The dorsalis-pedis pulsation was bilaterally palpable.

The laboratory data, in view of the subsequent course, were of considerable interest. Of two routine urine analyses, the highest specific gravity was 1.008, and the sediment on one occasion showed 2 red blood cells in thirty fields. The red-cell count was 3,930,000, with a hemo-

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globin of 11.6 gm. (80 per cent Sahli), and the white-cell count was 12,200, with 73 per cent polymorphonuclear cells (10 per cent band forms) and no eosinophilia. Blood chemical findings included a nonprotein nitrogen of 27 mg., a urea nitrogen of 11 mg., a sugar of 99 mg. and a cholesterol of 195 mg. per 100 cc. Total protein on admission was 7.1 gm., with albumin 3.7 gm. and globulin 3.4 gm. The blood-sodium level was 321 mg., and the chloride 295 mg. per 100 cc. The serologic findings were negative.

During the hospital stay of 7 days, the patient's oral temperature reached an average of 99.4°F. daily, with a pulse rate usually of 90, and respirations of 20. A diet with a calculated salt intake of 5 gm. daily was ordered, and an actual intake of 3.2 gm. was maintained after the 1st hospital day. During the first 4 days the fluid intake was high, and there was a diuresis averaging more than 3500 cc. daily, the total urinary chloride exceeding 4.65 gm. Thereafter, fluid intake and output fell to normal levels, and the total urinary chloride was 1.40 gm. The 24-hour urinary creatine varied from 89 to 35 mg., and the creatinine from 1013 to 486 mg. The blood pressure, taken at frequent intervals, showed a gradual decline, reading 95/60 on discharge. The wrist was treated with hot, Epsom salt soaks, and the subsiding infection of the foot with hot, boric acid compresses and elevation. Both regions improved rapidly. It was considered that the blood-pressure readings, the levels of sodium and chloride in the blood, and the normal 24-hour urinary chloride excretion on a diet fairly low in salt were sufficiently significant to eliminate the diagnosis of Addison's disease.

The patient experienced pain and constant edema in the ankles during the next 3 months. She developed numbness in the left side of the face and about her mouth, aggravated by cold. The mouth itself felt puckered, and the tongue tingled, without any relief after taking nicotinic acid. For 3 weeks before the second admission to the hospital, the swelling of the ankles had increased considerably, and the patient developed dyspnea and orthopnea, with a loose croupy cough.

The patient was admitted for the second time on November 22, 1939, when she appeared very ill, dyspneic and orthopneic, with pale and slightly cyanotic lips. The scleroderma and pigmentation were unchanged. The fundi were normal. There were signs of fluid in the chest on both sides posteriorly below the 7th interspace, extending well forward into the axillas. The apex impulse of the heart was palpable at the left anterior axillary line in the 5th interspace, and there was slight enlargement to the right. By percussion, no increase in supracardiac dullness was apparent. The heart action was regular and rapid, and the rate was 110, with sounds of fair quality; there were no murmurs. The pulmonic second sound was louder than the aortic second, and the blood pressure was 148/102. The abdomen was not remarkable except for tenseness suggestive of ascites. Neither the liver nor the spleen could be felt. There was marked edema of the lower extremities to the mid-thigh, and moderate pitting edema of the sacrum.

Laboratory studies showed a urine concentration varying from 1.010 to 1.020, with a very slight trace to trace of albumin, the sediment containing a few white cells, rare red cells, 2 to 4 granular casts and 1 or 2 hyaline casts per high-power field. The red-cell count was 3,720,000, with a hemoglobin of 10.2 gm. (70 per cent Sahli), and the white-cell count was approximately 18,000, with 87 per cent polymorphonuclears. A stool examination was negative for occult blood. The blood nonprotein nitrogen was 42 mg. per 100 cc. on admission, and 62 mg. 2 days later. The blood cholesterol was 255 mg. per 100 cc., the sugar 120 mg., the carbon dioxide combining power 56 vol. per cent, the total protein 6.0 gm., the albumin 3.3 gm., and the globulin 2.7 gm. per 100 cc. The blood-chloride level was 440 mg. per 100 cc. X-ray study revealed enlargement of the heart, chiefly to the left, with diffuse haziness of the lung fields and mottling at the bases interpreted as showing congestive changes. The electrocardiogram revealed normal rhythm, a rate of 110, left-axis deviation, notched and widened QRS complexes, probable intraventricular block, deep S_2, diphasic T_1, elevated ST_3 and ST_4, and a PR interval of 0.2 second.

On admission, the temperature was 100°F. by mouth, and rose to 101° before exitus. The pulse averaged 110 to 120, and the respirations 20. The patient was seen by a consultant, who wrote, "I believe that this woman is suffering from a diffuse arterial pathologic process that falls into the lupus erythematosus group." Treatment included high-vitamin diet, restriction of fluids, digitalis, and thiamin chloride intramuscularly and intravenously. On the night of the 2nd hospital day, the patient experienced an attack of pulmonary edema, which responded to morphine, atropine, tourniquets, venesection and oxygen by Boothby mask. On the following day, 750 cc. of thin amber fluid was removed from the right pleural cavity. The circulation time by the calcium gluconate method was 19 and 22 seconds. No diuresis resulted from the intravenous injection of 1 cc. of Mercupurin, nor from the similar administration of hypertonic glucose solution. The patient became semicomatose, developed marked difficulty in getting air in and out of the lungs, had convulsive twitchings, and died on the 5th hospital day.

Autopsy: The body showed good development and fair nourishment. Marked pitting edema was present in both lower extremities, extending almost to the crests of the iliums. In the exposed portions of the body, the skin was taut, inelastic and a shiny tan brown. This brownish pigmentation was most marked on the face and neck and over a collarlike area on the upper thorax. On the under surface of the tongue the mucous membrane had an irregular brownish pigmentation, and both buccal mucosas had small minute spots of brownish pigment. No lymphadenopathy was found. The fingers bilaterally revealed a peculiar firm nodularity of the terminal phalanges, not quite typical of clubbing. The skin in these areas was taut, tense and hard. No evidence of muscular atrophy was noted in either the upper or the lower extremities. On section, the musculature was of firm consistence and dark red brown.

There was 200 cc. of clear, straw-colored fluid in the peritoneal cavity, a total of 700 cc. in both pleural cavities, and 300 cc. in the pericardial sac.

The heart weighed 285 gm. and was increased in size, with moderate dilatation of the right side and definite hypertrophy of the left ventricle. The myocardium everywhere was of firm consistence. The valves and mural endocardium were normal. After injection and dissection, the coronary vascular tree appeared to be patent throughout both sides of the heart. The left ventricle measured 1.6 cm. in thickness, the right ventricle 0.5 cm.

The lungs, except for a small portion of each upper lobe, were solid and firm in consistence, with no palpable crepitation.

The spleen, which was of rather firm consistence, weighed 145 gm.

The liver weighed 1540 gm. and appeared normal except for slight congestion about the central areas.

Each kidney weighed 145 gm. The fibrous capsules

were thin, and stripped easily. The outer surfaces were smooth red gray, a slight fine granularity being visible and palpable. The cut surfaces were markedly congested, and the blood vessels stood out quite prominently in the cortex and the medulla, which were sharply demarcated. The cortex measured approximately 0.8 cm. in width; it was of uniform appearance, and the glomeruli were seen as minute pin points. No degeneration in the tubular regions was noted.

Both adrenal glands were of normal size and shape, with normal appearance on section. The remainder of the organs, including the thyroid and parathyroid glands and the brain, were not remarkable.

Cultures of the heart's blood and the pericardial fluid were sterile.

At microscopic examination, sections of the heart revealed extensive diffuse fibrosis throughout, especially marked on the right side. In some parts of the right ventricle most of the heart wall consisted of a condensed stroma and old avascular fibrous tissue, with scattered, small, slightly sclerotic blood vessels traversing the sheet of dense fibrous tissue. No acute arterial lesions were present in any of the sections, and there were no changes

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FIGURE 1. *Acute Necrotizing Arteriolitis and a Glomerulus with a Thickened Basement Membrane.*

suggestive of old healed arterial lesions, although the walls of the small arteries and arterioles revealed slight edematous thickening of their muscular coats. The valves were normal.

In the lungs, there was a diffuse pneumonic process, showing all stages of consolidation. Throughout the pulmonary tissues, the smaller blood vessels showed slight thickening, with edema of the medial muscular coats. In some places, one could note a ring of vacuoles, which appeared to separate the intimal coat from the media. Various sections revealed some fibrosis throughout the pulmonary tissue.

The arterioles about the adrenal capsule showed a slight but definite sclerosis of their walls. The parenchyma and cortex, however, were normal.

All sections of the kidneys revealed a diffuse acute and subacute necrotizing arteriolitis (Fig. 1). The glomeruli were not decreased in number, but were swollen and increased in size, the swelling being especially marked in the basement membranes about the capillary loops in the tufts, which were widened and had a hyaline appearance. The afferent arterioles likewise were more prominent, owing to swelling of their basement membranes, but there was no chronic hyalinizing arteriolar sclerosis. The acute necrotizing inflammatory process chiefly involved a medium-sized artery about the size of an interlobular artery. This reaction could be seen to spread into the afferent arterioles and then up into the capillaries of the glomeruli. The intimal coat was swollen and revealed

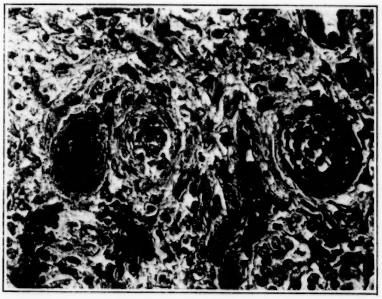

FIGURE 2. *Three Stages of Arteriolitis.*

The arteriole on the extreme left is similar to that in Figure 1. Note the thickened wall and the cellular proliferation in the arteriole at the extreme right.

marked proliferation of its cells, with marked narrowing of the lumen of the vessel. In many areas the walls of the arteries were edematous and necrotic, and were the site of deposits of purple-staining crescents of fibrin, with scatterings of polymorphonuclear cells. Several sites of rupture of the necrotic muscular medial coat of the artery, with exudation of polymorphonuclear cells into the surrounding stroma, were found. In other areas, this acute process appeared to be in the stage of healing, with lymphocytes predominating in the inflammatory infiltration and fibroblasts obliterating the vessel lumen. There was evidence of a completely healed stage, with small canalizing lumens that traversed the occluding mass of fibrous tissue within the former lumens of the vessels (Fig. 2). The tubules, as a whole, were slightly dilated, and their epithelial cells swollen and granular. There was only one wedge-shaped area of acute necrosis.

The parathyroid and thyroid glands were normal in all sections.

Sections of skeletal and diaphragmatic muscle presented no abnormalities of cells, stroma or blood vessels.

The epidermis revealed no atrophy, but the basal cells contained an increased amount of pigment. The dermis itself was slightly thickened. Scattered, otherwise normal, capillaries had a collar of lymphocytes about them. No degenerative changes in the collagen or elastic fibres could be seen.

The remainder of the sections, including those of the brain and cord, showed nothing worthy of remark.

The anatomic diagnoses were: acute and subacute necrotizing arteritis of kidneys; diffuse fibrosis of myocar-

dium; pigmentation of skin; chronic passive congestion of lungs and spleen; and confluent bronchopneumonia.

In many of its features, this case illustrates the classic characteristics of scleroderma. The history of Raynaud's disease, the sclerodactylia, the symptoms of arthritis with x-ray confirmation, and the temporary improvement with thyroid medication are typical. The sensitivity to sunlight, however, as manifested by deep and persistent bronzing of the exposed surfaces, was unusual, and reminiscent of the even more striking sensitivity noted in dermatomyositis and systemic lupus erythematosus. So intense was the pigmentation that the first hospital admission was for the express purpose of evaluating the possible presence of Addison's disease. A similar situation prevailed in the case reported by Talbott and his colleagues.[1] It is significant that throughout the first hospital stay the patient's temperature reached 99.4°F. daily and the pulse 90 while the patient was resting in bed, even after the minor local infection in the foot had completely subsided. This was definite evidence of a systemic reaction not usually seen in scleroderma. Evidence of renal involvement at this time was lacking; the urine analysis was negative, the nonprotein nitrogen of the blood was within normal limits, and the blood pressure was not elevated. Excretion of creatine, as often noted in scleroderma and dermatomyositis, was increased. At the time of the second hospital admission, three months later, failure of both the right and left sides of the heart was evident, and there were the albuminuria, microscopic hematuria and casts, and terminal azotemia seen in systemic lupus erythematosus and polyarteritis nodosa.

At post-mortem examination the extensive myocardial fibrosis, with adequate coronary circulation, and the pulmonary fibrosis were arresting findings, and recalled the marked increase in the connective tissue of the viscera reported by Matsui[2] in his cases of scleroderma. The striated muscle was normal. Neither the adrenal nor the parathyroid glands showed pathologic lesions. The kidneys in gross seemed essentially normal except for congestion, but microscopically they revealed widespread acute and subacute arteriolitis such as one would expect to find in a fulminating case of systemic lupus erythematosus. In this patient, the two basic pathologic changes of scleroderma — proliferation of connective tissue and alterations in the arterioles — were manifested in various internal organs. A case of diffuse scleroderma with identical changes in the renal arterioles, but without the visceral fibrosis, was reported by Masugi and Yä.[3]

Scleroderma

Credit has been given to Curzio, of Naples, for the first description of an authentic case of scleroderma in 1752.[4] The condition occurs most frequently in the fourth and fifth decades, although people of all ages may be affected. The female sex predominates at least in the ratio of 2:1. The onset may be slow, — with prodromal symptoms of malaise, joint pains, asthenia and loss of weight, — or rather sudden, following a systemic infectious disease such as influenza. Other cases appear insidiously after a long history of Raynaud's disease. A smaller number of cases have followed acute arsenism. Two forms are recognized. The circumscribed type may consist of small patches of thickened skin, often about the neck (morphea), linear streaks along the course of nerves or blood vessels and sclerodactylia involving the fingers, usually in association with Raynaud's phenomenon. The diffuse form may arise from the circumscribed, or may appear first as a widespread involvement. Progressing with variable speed through the three stages of edema, induration and atrophy, the affected areas become brawny and hidebound. Pigmentation is common, from an ivory or yellowish tint to a deep bronze, especially over the exposed portions of the body, where it is indistinguishable from Addisonian coloring. Cutaneous sensation and both deep and superficial reflexes are usually well preserved. In half the generalized cases, the pain, swelling and stiffness of the joints simulate a severe and extensive arthritis. Atrophy of voluntary muscles, with contractures about the joints, serves further to limit motion. Involvement of the muscles of the tongue, soft palate and larynx is not uncommon. In one third of the cases, vasomotor disturbances are prominent. Calcification in the skin, often in the form of nodules, has been repeatedly noted. The eye grounds are normal. Aside from the progressive weakness and loss of weight, there are usually no constitutional symptoms until late in the disease. There is no fever, or any characteristic change in the blood other than a mild anemia. The basal metabolic rate is normal, and the blood calcium and phosphorus levels are usually not significantly altered. X-ray films of the hands are usually interpreted as showing osteoporosis and arthritic changes. Urinary excretion of creatine is definitely increased.[5] The course may be measured in weeks or years, and remissions are not unusual.

The pathology, extensively studied by Matsui,[2] is not limited to the skin, but affects all the viscera of the body, although one or more of the organs show a predominance of findings. The two

characteristic processes are proliferation of the connective-tissue stroma and changes in the small arterioles. The thickening of the connective tissue leads to rupture and disappearance of elastic fibers. In the blood vessels, there may be hypertrophy of the smooth muscle of the media, with infiltration of connective-tissue fibers, a thickening of the intima, with narrowing of the lumen, or complete obliteration, with thrombus formation. The changes in the skin and subcutaneous tissues exemplify both these processes. The epidermis is only slightly altered, whereas the corium shows hypertrophy of collagenous tissue, with obliteration of the papillas and replacement of fatty tissue, compression and atrophy of the sweat glands and hair follicles, and an obliterative endarteritis, with thickening of the media and adventitia and perivascular lymphocytic infiltration. There is atrophy, with similar changes in the voluntary muscles, subjacent or farther removed, and some general osteoporosis more marked in the affected regions, especially the terminal phalanges. The bone marrow becomes aplastic. Fibrosis of the lungs may occur and may result in pulmonary hypertension and dilatation of the right side of the heart. The kidneys often show changes in the blood vessels, with or without sclerosis of the glomeruli, tubular degeneration and general fibrosis. One or more of the endocrine glands commonly manifest atrophic or sclerotic changes.

Studies on the etiology of scleroderma have followed four main channels: endocrine dysfunction, vascular changes, disorders of the nervous system, and miscellaneous toxic and infectious agents.

The finding at autopsy of alterations in one or another of the endocrine glands, especially the pituitary and the thyroid gland, and the clinical evidence of glandular imbalance, occurring concomitantly in cases of scleroderma, have tended to implicate the glands of internal secretion. Matsui,[2] noting a diminution in the chromogenic cells of the pituitary gland, stressed its role in the pathogenesis. Others,[6] because of the Addisonian pigmentation and myasthenia, have suspected the adrenal glands. Most observers,[7–9] however, have considered the changes in function and histology of the endocrines to be secondary manifestations of the disease. They point out that scleroderma occurs with both hyperthyroidism and hypothyroidism, and consider that the beneficial effects that sometimes follow the use of thyroid medication are due to its local effect on the circulation of the skin and its general effect on metabolic processes. On the other hand, Leriche and Jung[10] maintain that scleroderma is a cutaneous form of chronic hyperparathyroidism, and advance considerable laboratory and clinical evidence in support of their views. In young pigs and rats, the injection of parathyroid extract has reproduced the disease. The calcium content of the skin in scleroderma is greatly increased, whereas the bones show osteoporosis. Surgical removal of the parathyroid glands in patients with scleroderma has resulted, according to Leriche and his associates,[11] in considerable improvement in most cases, and microscopic examination of the resected tissue usually shows hyperplasia. Leriche summarizes his opinion in the statement that the parathyroid glands are the primary, the bones are the intermediate, and the skin is the final site of the disturbance. Nevertheless, the data from metabolic studies are somewhat at variance with this concept. In hyperparathyroidism, the blood phosphorus content is low, the calcium is usually elevated, and urinary excretion of calcium is increased. In scleroderma, the blood levels of phosphorus and calcium are usually normal, and a negative calcium balance is lacking. The calcinosis of tissues may be due to local causes rather than to general hyperparathyroidism, and the osteoporosis is often confined to the affected regions.

The evidence that vascular changes play an important role in the causation of scleroderma is plentiful and impressive. Locally, the common association with Raynaud's disease, and the histologic demonstration of endarteritis and perivascular round-cell infiltration are classic features recognized by all investigators.[2, 4, 7, 9, 10, 12, 13] Stokes[8] has considered that the basic disturbance is an endarteritis, the huge increase in connective tissue being essentially a fibrosis such as follows reduction in blood supply. That this lesion of blood vessels is fundamental and widespread, and not confined merely to the skin and underlying tissues, is indicated by the autopsy reports published by numerous observers.[2, 14–16] Marinescu and his co-workers[14] reported 5 cases of scleroderma, one of which at autopsy showed extensive arteriolar changes in the skin, heart, kidneys, nervous system and other organs. Matsui[2] described a case, with marked arteriolar changes in the kidneys and, to a lesser degree, in various other organs. The case reported in this paper offers further evidence along these lines.

The high incidence[12] of Raynaud's phenomenon in scleroderma has drawn attention to the part that the sympathetic nervous system plays in the disease. Brown and his associates[17] have investigated the factors of vasospasm and local disturb-

ances in the capillary bed. They found a sharp diminution in the number of open capillaries per unit area of skin, with the blood flow easily disturbed or slowed to a stop by lowering the temperature several degrees. The capillary loops were large, distorted and irregular, with outlines frayed and indistinct. They believed that although changes in vasomotor tone were important in scleroderma, they were not the primary cause. Clinically, the effects of sympathectomy and of Mecholyl iontophoresis have in some cases been beneficial. Sympathectomy has resulted in improvement in some cases not previously benefited by removal of the parathyroid glands, and the reverse has also been true. Lewis and Landis,[18] however, on the basis of considerable experimental study, believe that the role of the sympathetic nervous system is much less significant than purely local functional and structural changes in the digital arterioles in the circumscribed form involving the fingers.

Data concerning the relation of infectious and toxic agents to the pathogenesis of scleroderma are almost entirely clinical. The onset after erysipelas, hepatic infections and rheumatic states has led to the theory that the disease is a sequel of many infectious diseases. The appearance of scleroderma after acute arsenism or plumbism and the reports of increased amounts of arsenic or lead in the skin in some of these cases have inclined some observers to raise the question of a toxic origin of the condition.

Dermatomyositis

First described in 1887, independently by Hepp,[19] by Wagner[20] and by Unverricht,[21] who gave it its name, dermatomyositis presents a clinical syndrome that may vary widely. Most commonly it affects people of middle age, with children next in frequency, but cases at all ages and in both sexes have been described. There is usually an insidious onset, with prodromal symptoms for several weeks consisting of weakness, general malaise, anorexia or vomiting. The diagnostic triad of edema, dermatitis and myasthenia then appears, each varying in degree from case to case. In one fourth of the patients there is erythema and edema of the eyelids and face. The skin rash may be widespread, and usually possesses a peculiar heliotrope coloring often noted in disseminated lupus erythematosus. The eruption has been variously described as erysipeloid, roseolar, morbilliform, urticarial, eczematous and petechial, and may first appear after exposure to sunlight. In swift succession, manifestations of muscle disturbances follow. There are symmetrical muscle weakness, tenderness, swelling, brawny edema and pain on active and passive motion. The patient may be rendered helpless. The muscles, firm and tense or soft and boggy, may be involved at a distance from the skin lesions. The skeletal muscles, especially those of the limbs, are chiefly affected, but in severe cases involvement of the muscles of deglutition, speech and respiration may result in symptoms resembling bulbar palsy. Splenomegaly is not uncommon. The temperature is usually remittent from a level of 101°F., but may exceed 103° or fever may be entirely absent. Tachycardia out of proportion to the temperature is often noted. An elevation of the white-cell count is usual, with eosinophilia in approximately one fifth of the cases. The urine often contains albumin, with pronounced creatinuria. The mortality averages 50 per cent, and death may occur from pneumonia, pleurisy or pericarditis. If the patient survives this stage, the edema subsides and the degenerative and inflammatory reactions in the muscles and skin may proceed to atrophy, fibrosis and contractures, especially at the elbows and knees. Osteoporosis occurs late, and the skin may take on a boardlike thickening identical with that observed in scleroderma. In mild cases, remissions or complete recovery may take place.

The pathology in the early stages, as determined by biopsy, is indistinguishable from that of early scleroderma. The skin, subcutaneous tissue and muscles are involved. The picture is one of edema, swelling of the endothelial cells lining the vessels, and perivascular and diffuse infiltration by lymphocytes and plasma cells.[16] Keil[22] has stated that in many cases of dermatomyositis the fundamental pathologic alteration occurs in the vasculature, with secondary implication of the muscle parenchyma. Numerous observers have expressed similar views, but there is no general agreement on this point. The muscle fibers present various disintegrative changes, ranging from swelling and loss of cross striations to vacuolar or hyaline degeneration. The similarity to the findings in thyrotoxicosis and myasthenia gravis has been noted.[23] According to Brock,[24] biopsy at a later stage in scleroderma shows thick-walled vessels, with the lumens narrowed or occluded, and an increase of the connective tissue in the sheaths and interstitial spaces of the muscles, with subsequent myosclerosis, whereas in dermatomyositis the cellular infiltration and degeneration of the muscle parenchyma itself persist to the end and the vascular changes are minimal. This observer found a diffuse increase in connective tissue in the heart at one post-mortem examination.

Various features of the disorder have suggested an inflammatory or infectious etiology.[25] The frequent occurrence of first symptoms after a fe-

brile disturbance such as tonsillitis and influenza, the fever, albuminuria and splenomegaly in some cases and the relapsing character of many cases all appear to point in this direction. Bacteriologic studies, however, have been almost uniformly negative. Keil[22] has discussed the factor of lead as a vascular poison in the pathogenesis of this and similar diseases, citing cases from his own experience and from the literature, but the evidence is based on association and analogy and is not entirely convincing. The concept that dermatomyositis may be a primary disturbance of the blood vessels was first proposed by Lépine,[26] who suggested the term "angiomyositis." Köster,[27] in a report of a series of cases with microscopic data, emphasized repeatedly the importance of the blood vessels in the pathogenesis of the condition. Fahr[28] also believed that in many cases of dermatomyositis the initial fundamental disturbances are in the blood vessels supplying the affected muscles, the alterations being a form of necrotizing arteriolitis. Equally significant is the relation of dermatomyositis to scleroderma. The cardinal pathologic alterations in the blood vessels and connective tissue of skin, muscles and other organs are considered identical in both conditions, although varying in degree and distribution.[23, 29] Other observers, however, do not agree with this opinion. Clinically, the evidence of a close relation is so impressive that many consider the two conditions as one disease. The literature since 1900 is replete with records of carefully observed cases diagnosed and reported as scleroderma, later assuming the classic feature of dermatomyositis, and the reverse has occurred even oftener.[23–25, 30] Many transitional cases are also reported.[16, 31, 32] In both diseases, a history of antecedent Raynaud's disease is common, edema is an initial symptom, joint pains are present, the pharynx and larynx may be affected, creatinuria is present, renal involvement with albuminuria may be evident, and calcification or pigmentation may occur. The diagnostic difficulties have been commented on by Brock,[24] who found that even biopsies were misleading until late in the disease. Without a biopsy of muscle the differentiation of dermatomyositis from trichinosis may be impossible. In the latter, involvement of the eye muscles and diaphragm occurs much more commonly than in dermatomyositis.

Disseminated Lupus Erythematosus

In his memorable reports of an "erythema group" of diseases with visceral manifestations, Osler[33] contributed greatly to the evolution of the present concept of systemic disease associated with cutaneous manifestations. Of such syndromes, acute and subacute disseminated lupus erythematosus (as distinguished from the fixed and generalized discoid types) is a notable example. First described by Kaposi[34] in 1872, this disease shows a marked predilection for females, usually in the second to fourth decade of life. Nevertheless, cases have been reported in both sexes, at all ages and in many races and countries. Constitutional symptoms may far overshadow the cutaneous eruption, and often precede it for weeks or months. There may be a prolonged and insidious onset, with fatigue, exhaustion, disability, low-grade fever and joint pains, often diagnosed as rheumatoid arthritis or rheumatic fever. With the appearance of skin lesions or signs of visceral disturbances, the true nature of the serious underlying condition becomes apparent.[35] In the fulminating case, the constitutional and skin manifestations appear abruptly and simultaneously, the temperature exceeds 103°F., prostration is extreme, the sensorium is clouded, and stupor or delirium occurs. The dermatitis usually begins on the face or upper part of the thorax and neck as areas of indefinite superficial erythema that coalesce and become well demarcated. Edema of the eyes and face is often marked. There is rapid extension to the extremities, with involvement of the finger tips. The eruption, favoring the exposed surfaces, is bright reddish violet, often with a cyanotic tinge in the active areas. Petechial, purpuric, papillar or bullous lesions are seen, but indurated plaques with epithelial plugging, scaling and atrophy are rare. When involution occurs, residual pigmentation of various types may follow, and may simulate the extensive deep pigmentation of Addison's disease. Undue exposure to sunlight has precipitated the first appearance of the rash and an intensification of the constitutional reaction in a considerable number of cases. Local or generalized adenopathy is described. The systemic symptoms are almost infinite in variety. Involvement of the serous surfaces, including synovia, pleura, pericardium and endocardium, is common. Pain in the form of arthralgia, myalgia and neuralgia appears early and may be severe. Gastrointestinal symptoms vary from nausea, vomiting and diarrhea to crises of abdominal pain at times so marked as to result in surgical exploration. In a small proportion of the cases, the spleen is enlarged. In some cases, ophthalmoscopic examination reveals perivascular hemorrhages and fluffy exudates. Evidence of renal damage, with albuminuria, microscopic hematuria and casts, is a feature of the condition, but the blood pressure is usually not significantly elevated. Terminal

azotemia is frequently noted, and nephrotic syndromes have been described. The urinary findings are not consistently characteristic of any one type of renal lesion. There is often depression of the bone marrow, with secondary anemia, leukopenia and thrombopenia, a rise in the white-cell count usually signalizing a serious and terminal complication. Serologic tests for syphilis may be falsely positive. Cultures of the blood have given equivocal results. The course in the acute fulminating cases is progressively downward, whereas in the more chronic types recession of the eruption and of the constitutional symptoms occurs only to be followed by an exacerbation months later. The mortality exceeds 90 per cent in the acute cases, and averages 50 per cent in the milder forms. Death may result from pneumonia, pericarditis, meningitis or uremia. The prognosis is indicated more accurately by the severity of the general reaction than by the extent of the cutaneous processes, which are helpful in diagnosis.

The characteristic pathologic features are found in the minute blood vessels, and consist of widespread proliferative changes in the endothelium, with a tendency to thrombus formation, or of a degenerative or necrotizing process in the walls, often with hemorrhage into adjacent tissues. These changes, however, are not specific for any one disease. In disseminated lupus erythematosus, the changes in the skin are of minor importance and without diagnostic significance.[36] Thinning of the epidermis, atrophy of the sebaceous glands and hair follicles, edema of the cutis and marked dilatation of the superficial blood vessels and lymph spaces, with extravasation of blood and serum, are the essential findings. Most striking are the lesions in various organs throughout the body, especially the kidneys, heart, lungs, liver and serous surfaces. Considerable variability is seen in the general distribution of these lesions and in the viscera principally affected, but the kidney is most frequently involved. In gross these organs usually show little of significance, and have been discarded frequently without investigation. Microscopic study reveals hyaline thickening of many glomerular afferent vessels, with secondary thrombi, fibrosis and recanalization. The glomeruli themselves may be implicated, with a homogeneous thickening of the capillary wall described as a "wire-loop" effect.[37-41] At times a focal or diffuse panarteritis is found, with involvement of all the coats of the vessels, necrosis of the media, proliferation of the intima, secondary thrombi and periarterial accumulations of cells.[42-44] Stickney and Keith[45] found the renal arterioles to be essentially normal in most of their cases, whereas the glomerular capillaries showed proliferation of the endothelial cells, hyaline thickening of the capillary walls and changes in the basement membrane, similar to the alterations in the toxemias of pregnancy, ulcerative colitis and peritonitis. Renal lesions were also noted by Snapper,[46] O'Leary[47] and Montgomery,[48] who commented on their similarity to the findings in eclampsia. In a considerable proportion of the cases, there is an endocarditis of varying type, with and without associated Aschoff bodies in the myocardium. Pericarditis, pleurisy, synovial changes, splenic infarcts, hepatic and gastrointestinal lesions, and terminal pneumonia constitute the remaining predominant changes seen post mortem.[49] On the other hand, Montgomery[50] was unable to discover any characteristic obliterative changes in the smaller blood vessels either in the internal organs or in the skin, and Mallory[51] has found no lesion that he considers pathognomonic of disseminated lupus erythematosus.

The etiology of the disease remains unknown. Innumerable theories have been advanced to explain its pathogenesis. Most observers favor the view that it is an infection, perhaps streptococcal, and others stress the relative frequency of a tuberculous background. Goeckerman[52] has considered it as a response to a septic infection conditioned by a previously established tuberculous allergy. O'Leary,[53] however, believes that the disorder is due to a toxemia, probably attributable to a bacterial agent. The frequent recovery of the tubercle bacillus in blood cultures, as reported by some investigators, has not been confirmed. Tuberculous adenitis is surprisingly prevalent. Streptococci of various types are often isolated in the terminal stages, but their primary role is open to doubt. The condition has been attributed to trauma in the form of drugs and heat, sensitivity to light, toxic factors, various metabolites, focal infection, disease of the bone marrow and disease of the reticuloendothelial system. Ludy and Corson[54] believe that the action of ultraviolet light in constitutionally susceptible people is a factor, and that a heavy metal like lead may serve as a catalyst. In almost half their cases, they found hematoporphyrinuria, but the attempts of numerous other investigators to detect this substance in the urine have been unsuccessful. The common observation that signs of a prolonged and severe systemic disturbance have antedated the appearance of the skin lesions indicates that sunlight can have only the secondary effect of determining the onset and localization of the dermatitis. The problem is whether disseminated lupus ery-

thematosus is a pathologic entity due to a specific if unknown cause, or whether it is a peculiar reaction of the internal organs and skin initiated by a variety of different agents. Madden[55] regards the various clinical forms as manifestations of one disease, differing only in the severity and distribution of the lesion. Denzer and Blumenthal,[41] recognizing that the vascular changes are the only conspicuous pathologic finding, nevertheless refuse to regard them as the sole basis of the disease and postulate an underlying more fundamental pathologic disturbance.

Although the disease is commonly considered as a problem for the dermatologist, the internist may see these patients first if the systemic complaints precede the onset of the dermatitis, if the skin eruption is mild and inconspicuous, or if the clinical course is fulminating, with severe constitutional symptoms. Diagnosis, as Mook and his associates[38] point out, is elusive and difficult. When the cutaneous manifestations predominate, a variety of skin diseases are simulated. If the systemic reaction is marked, typhoid fever, pyemia, malignant endocarditis and rheumatic fever must be considered. During crises of abdominal symptoms, surgical intervention for possible appendicitis, cholecystitis or perforated duodenal ulcer has seemed imperative.

The relation of systemic lupus erythematosus to dermatomyositis, and less directly to scleroderma, is suggested and supported by both clinical and pathological evidence. Raynaud's phenomena may precede or accompany the disease in all three. Subcutaneous calcification and pigmentation on the exposed surfaces, reaching Addisonian intensity, may occur in all three. There is hypersensitivity to sunlight with aggravation of the condition in both systemic lupus erythematosus and dermatomyositis. There are numerous reports[19, 56] in the literature, of which only a few are cited, describing cases diagnosed as disseminated lupus erythematosus by one or more competent dermatologists and later showing the typical features of dermatomyositis. Turner[57] reported a definite case of dermatomyositis that in a recurrence exhibited the skin lesions and constitutional symptoms of lupus erythematosus disseminatus. Montgomery[36] has also pointed out the clinical similarities of these two conditions. Dowling[23, 31] considers that the vascular changes of scleroderma and dermatomyositis are of the same order, and much like those of disseminated lupus. Visceral lesions, with involvement of the smaller blood vessels, occur in all three conditions.

The Libman–Sacks Syndrome

First described in 1924, the features of the Libman–Sacks[58] syndrome were listed as prolonged fever, an atypical verrucous endocarditis, absence of Aschoff bodies in the myocardium, white-centered petechiae in the skin, signs of renal disease and consistently negative blood cultures. In several patients, skin lesions indistinguishable from those of disseminated lupus erythematosus were noted. In 1931, Baehr,[59] discussing the renal lesions seen in 17 cases, reported that unusual vascular changes were found not only in the kidneys but in other internal organs, and that most but not all cases had skin manifestations characteristic of disseminated lupus. The syndrome then included pleural effusion, pericarditis, arthritis and leukopenia. By some observers it was considered as a separate entity; others regarded it as one of Osler's erythema group, and a few included it in the many variables of subacute disseminated lupus erythematosus. In a subsequent paper Baehr[40] detailed the clinical and pathological data in 23 cases of disseminated lupus, in 13 of which the coarse verrucous endocarditis of the Libman–Sacks syndrome without Aschoff bodies was found. Twenty of these cases presented disseminated vascular lesions in the kidneys and other viscera. It was then apparent that endothelial damage, which might involve the valvular endocardium or not, was the outstanding feature of this group of cases, and the unusual endocarditis that originally drew attention to the syndrome assumed a position of secondary importance. In his pathological studies of systemic lupus, Montgomery[48] found endocarditis in 7 of 15 cases, in each one associated with Aschoff bodies in the myocardium. Belote and Ratner,[60] Denzer and Blumenthal,[41] Keil[61] and Montgomery[36] have identified the Libman–Sacks syndrome more or less definitely with disseminated lupus erythematosus. It is of interest that it has never been reported in scleroderma or dermatomyositis.

Polyarteritis Nodosa

Under the name "periarteritis nodosa" a voluminous literature has accumulated concerning a disease characterized by widespread segmental lesions in the smaller arteries and arterioles. Occurring at all ages, but most commonly between ten and forty, the condition affects males four times as frequently as females. The onset may be abrupt or gradual, with fever, muscular pains, general weakness, abdominal pain and edema. The temperature reaches 101°F., may be constant

or intermittent, and is associated with a tachycardia out of proportion to the temperature level. Polymyositis in the extremities and polyneuritis of peripheral type are common. Cramplike or colicky abdominal pain occurs in most cases. Nodules, firm and nontender, may appear in the later stages along the course of superficially placed arteries and thus establish the diagnosis on clinical grounds or by biopsy. Cutaneous lesions of many types are described. Leukocytosis, secondary anemia and albuminuria, with microscopic hematuria and casts, are almost constant features. Hypertension is a relatively late manifestation and is usually of renal origin. Later, there is cardiac failure without obvious cause, and bronchiolitis with prominent cough. The presenting symptomatology has been grouped as renal, abdominal, neuromuscular, cardiac and bronchial. The duration of the disease is usually measured in months, and the prognosis is extremely unfavorable.

With the recognition that the media rather than the adventitia was the primary seat of the lesion and that all the coats of the vessels were involved, Haining and Kimball[62] proposed the name "polyarteritis nodosa." In addition to inflammatory changes in the adventitia, Leishman[63] described necrosis of the media, rupture of the internal elastica lumina, proliferation of the intima and thrombosis, at times with recanalization. In the early stages, the characteristic local cellular reaction is a polymorphonuclear one, with a large percentage of eosinophils.[64] In order of frequency, the organs involved are the kidneys, heart, liver, spleen, lungs, mesentery, skeletal muscles and nervous system. O'Hare and his associates[65] have noted the resemblance of the pathology to that of the rickettsial diseases. Fahr[28] considered that the arteriolitis of dermatomyositis might be allied to that of periarteritis nodosa.

Suggestions concerning etiology include streptococci, syphilis, parasites, viruses and allergic factors. Two opposing schools of thought are exemplified by Moschcowitz,[66] who maintains that periarteritis nodosa is not a primary clinical or morphologic entity but a complication of various widely divergent conditions, and by Haining and Kimball,[62] who, believing that it is due to a specific infection, possibly with a virus, point out that if it is a manifestation secondary to infection it should occur much oftener.

Discussion

It is evident from the descriptions of these diseases that a differentiation on a clinical basis should be possible in most cases.

In scleroderma, there is a preponderant incidence in the fourth and fifth decades and in women; antecedent vasomotor disturbances in one third of the patients; the triad of edema, induration and atrophy of the skin; arthritic manifestations, localized osteoporosis and secondary atrophy of voluntary muscles; absence of fever or other constitutional symptoms until late; and a chronic course, with relatively favorable prognosis. Although changes in the small arterioles and proliferation of the connective-tissue stroma may be found throughout all the viscera and in many of the muscles, resulting systemic disturbances that can be detected clinically are relatively uncommon.

Dermatomyositis occurs more commonly in children as well as later in life, is preceded by prodromal symptoms, and presents a diagnostic triad of edema, dermatitis, with sensitivity to sunlight, and myasthenia. Muscular pain, tenderness and swelling are common. A constitutional reaction is evidenced by fever, tachycardia, albuminuria, leukocytosis, occasional eosinophilia and splenomegaly. The prognosis is guarded, with an average mortality of 50 per cent. The pathologic changes involve the small blood vessels and the musculature, the skin being secondarily affected in the typical cases.

Disseminated lupus erythematosus is seen classically, although not invariably, in females of the second to fourth decade, and is characterized by constitutional symptoms of smoldering or fulminating intensity that precede, follow or appear abruptly with the cutaneous eruption. As in dermatomyositis, exposure to sunlight may aggravate or initiate both the rash and the general symptoms. The prostration, fever, tachycardia, arthralgia, gastrointestinal symptoms and involvement of serous surfaces, together with evidence of renal disturbance and depression of the bone marrow, all indicate the severity of the systemic reaction. The ultimate prognosis is poor. The pathologic changes, which remain the subject of much controversial discussion, are not peculiar to this disease. There are widespread proliferative changes in the endothelium of the minute blood vessels, at times with degenerative or necrotizing processes in the walls, varying considerably both in intensity and in distribution in individual cases. In some patients, involvement of the endocardium with an atypical verrucous process has led to the description of the Libman–Sacks syndrome.

Polyarteritis nodosa is seen most commonly between the ages of ten and forty, and in males much more frequently than in females. The general systemic disturbance is characterized by fe-

ver, myalgia, leukocytosis, abdominal pain and renal involvement, with albuminuria, microscopic hematuria and casts. Cutaneous lesions may occur, but are easily distinguished from the eruption of dermatomyositis and disseminated lupus erythematosus. In some cases the appearance of nodules along the course of superficial arteries settles the diagnosis. The pathologic lesions consist of a segmental involvement of the small arteries and arterioles that starts usually in the media, involves all the coats of the vessels and leads to a characteristic local polymorphonuclear cellular reaction, with a large percentage of eosinophils. The kidneys are most markedly affected. The disease runs a downward course over a period of months.

Efforts to group the various conditions discussed in this report under the heading of diffuse vascular disease or mesenchymal disease have been criticized as an attempt at oversimplification that does not actually contribute to an understanding of the fundamental pathogenesis of these disorders. Differences do exist in the extent of the pathologic changes, the size of the vessels involved, the organs chiefly affected and the resultant clinical picture. Nevertheless, if it is recognized that the classification is a broad and tentative one, there can be no serious objection.

Three important and perplexing questions arise in a survey of these diseases. What is the essential significance of the changes in the blood vessels? What agents or mechanisms bring about these alterations? Are various members of this group different clinical manifestations of the same disease? One enters immediately on highly controversial ground.

Although the vascular pathology must be considered the most constant histologic finding, in many cases the changes are so slight and the distribution so limited that they scarcely explain the varied clinical pictures and the frequent fatal results. Occasionally no blood-vessel alterations whatever can be demonstrated, so that Mallory[51] and others have come to believe that there is no pathognomonic pathology in systemic lupus erythematosus and similar conditions. A conservative attitude, such as that of Denzer and Blumenthal,[41] seems best — namely, that the vascular lesions are merely a manifestation of an underlying pathologic process that in its progress frequently leads to morphologic changes in the small blood vessels.

Equally obscure are the etiologic agents causing these changes, and the mechanism by which the effects are produced. The very multiplicity of suggested factors indicates the confusion that surrounds this problem. The role of constitutional susceptibility is repeatedly stressed in the literature. An example of this concept is seen in systemic lupus erythematosus, which is attributed by some to a response to a streptococcal infection in a patient previously sensitized by tuberculous allergy. The possibility of some form of toxemia is given impetus by the similarity of the renal lesions to those found in some cases of eclampsia. Various observers maintain that these diseases are distinct entities produced by specific if unknown causes, and point out the resemblance of the vascular lesions to those seen in rickettsial diseases, such as typhus. On the other hand, it is generally agreed that polyarteritis nodosa can be a sequel to a number of infectious and toxic conditions.

Most disconcerting have been the cases, diagnosed by careful clinicians as typical of one disease, that have progressed and assumed the classic clinical and histologic features of another in the group. Many of these transitional cases are reported. The logical consequence of this transition has been the tendency to identify dermatomyositis with scleroderma, and disseminated lupus erythematosus with dermatomyositis. Since the diagnosis must almost always be a clinical one without the confirmation that laboratory tests might give, it is probable that most of these cases represent diagnostic errors demonstrated with the passing of time. All the diffuse vascular diseases possess many symptoms and signs in common, and the placing of undue emphasis on any one of these may lead to unwarranted interpretations and conclusions. It is clear that in the final stages, dermatomyositis may be associated with the atrophic cutaneous changes of scleroderma, and that advanced scleroderma may include the extensive muscle atrophy and degeneration seen in dermatomyositis. Most of the confusion between the latter condition and systemic lupus erythematosus has arisen from the character and distribution of the rash and the associated myasthenia. Until further information is available, it seems best to consider these several diseases as clinical entities and to regard a diagnosis in the early phases as only tentative.

Summary

Clinically, there are characteristic syndromes that correspond to the diagnostic terms of scleroderma, dermatomyositis, disseminated lupus erythematosus and polyarteritis nodosa. Not infrequently, however, patients present symptoms and signs that form essential characteristics of two or more of these conditions.

Since the diagnosis is almost always a clinical one without laboratory confirmation, the placing of undue emphasis on certain features may lead

to diagnostic errors and a tendency to identify one disease with another.

There is no unanimity of opinion regarding the specific and fundamental pathology of certain of these syndromes, all of which represent a widespread vascular involvement, differing usually in the extent of the pathologic change, the size of the vessels involved, and the organs chiefly affected.

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TUBERCULOSIS OF THE STERNUM*

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TUBERCULOSIS rarely involves the sternum. In 1134 cases of bone and joint tuberculosis admitted to the Lakeville State Sanatorium from 1926 to 1940, the diagnosis of tuberculosis of the sternum was made in only 12, an incidence of 1.1 per cent. References in the literature consist essentially in a few isolated case reports.[1, 2]

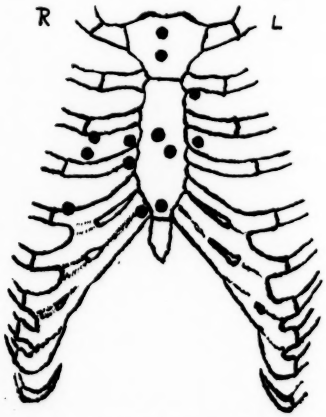

FIGURE 1. *Approximate Distribution of Sinuses in Patients with Tuberculosis of the Sternum.*

This paper presents a study of these 12 cases, 9 of which were followed for an average of more than five years.

The 12 cases were about equally divided as to sex: 7 females and 5 males. The ages of the patients at the onset of symptoms varied from one-and-a-half to seventy years, and there was no preponderance of any age group. In no case was there a history of trauma. There was a definite history of contact with tuberculosis, however, in 5 cases.

Tuberculosis of the sternum must be suspected when a patient who has a tuberculous focus elsewhere in the body develops a swelling on the anterior chest wall. Eleven of the 12 patients had other tuberculous lesions. A painless swelling in the region of the sternum was the presenting symptom in 7 cases, whereas pain was an early symptom in only 3. In 2 cases a discharging sinus was the chief complaint.

Eventually, practically every case develops one or more draining sinuses, and in about a third of the cases the sinuses are multiple. Figure 1 depicts the general distribution of these sinuses. It can readily be seen that any portion of the sternum or its adjacent structures may be involved; hence, the exact location of these sinuses is of no diagnostic significance.

Careful study of the material discharging from the sinuses, however, is essential. Indeed, it is often difficult to make a correct diagnosis before a sinus develops. Material that drains or is obtained at operation should be subjected to thorough pathological study, including guinea-pig in-

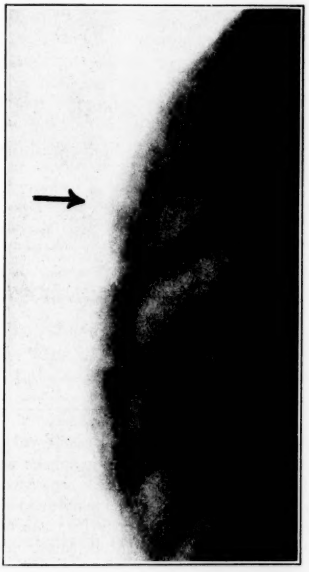

FIGURE 2. *Lateral View of Sternum in a Two-Year-Old Child (Case 12).*

Note the area of rarefaction in the manubrium. The lesion healed clinically and roentgenologically without operation.

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oculation. In 8 of the cases, such material confirmed the diagnosis of tuberculosis: 2 by guinea-pig test alone, 2 by biopsy alone and 4 by both methods. In 4 cases, the diagnosis was made only on clinical and roentgenographic evidence.

Tuberculosis of the sternum must be differentiated from tuberculosis of the chest wall and tuberculosis of the ribs and costal cartilages.[3] Tuberculosis may also involve the lymphatic vessels situated in the anterior costal interspaces, as well as the internal mammary or sternal lymph nodes, and necrotic nodes in this area may give rise to abscesses. In female patients, tuberculosis of the breast must occasionally be considered. The injection of a radio-opaque substance under such circumstances readily gives the clue to the actual process. A negative tuberculin test helps to distinguish chronic nontuberculous osteomyelitis of the sternum from tuberculosis and is therefore of value. Syphilis can be identified by the Wassermann test and by the fact that syphilitic lesions usually heal rapidly with specific treatment. Sarcoma of the sternum may simulate tuberculosis roentgenographically, according to Cella Malugani,[4] but since the sternum is readily accessible surgically, a biopsy specimen should be taken whenever there is the slightest doubt. Other tumors, such as cysts, lipomas and fibromas, may also be ruled out by biopsy.

TABLE 1. *Analysis of Cases.*

CASE NO.	SEX	AGE AT ONSET OF SYMPTOMS	PRESENTING COMPLAINT	OPERATION	PATHOLOGICAL CONFIRMATION OF DIAGNOSIS	ASSOCIATED TUBERCULOUS LESIONS	COMMENT
		yr.					
1	F	17	Discharge	Incision and drainage	No	Trochanter Kidney	Followed 2 10/12 years; no recurrence of disease of sternum.
2	M	10	Swelling	Incision and drainage, curettage, and biopsy	Yes	Lymph nodes Spine	Discharged in poor condition at parent's request; followed 2 7/12 years; then lost (probably dead).
3	F	10	Discharge	None	No	Lymph nodes Spine Lungs	Had one sinus which stopped draining one month after admission; followed 11 3/12 years; no recurrence of sternum disease; works as nurse.
4	M	19	Swelling	Aspiration	No	Ankle Lungs Bowel	Left at own request against advice; had two sinuses died 3 8/12 years later of pulmonary tuberculosis.
5	F	67	Swelling	None	Yes	Ankle	Sinus healed 2 years after discharge; patient later developed Pott's disease; followed 4 3/12 years; died of arteriosclerosis in an insane asylum.
6	M	22	Swelling	Aspiration	Yes	Finger Lungs	Had four sinuses in all; has not worked since discharge; followed 3 7/12 years; has far advanced pulmonary tuberculosis at present.
7	F	70	Swelling	Incision and drainage	Yes	Lymph nodes Ribs Pleura Lungs	Died 7 months after admission; autopsy revealed extensive tuberculosis of chest and arteriosclerosis.
8	F	40	Swelling	Excision of costal cartilage	Yes	Lymph nodes	Sinus healed 7 months after admission; followed 10 5/12 years; has had no recurrence of sternal disease.
9	F	26	Pain	Aspiration and resection of sinuses	Yes	Chest wall Peritoneum	Followed 10/12 years; slight drainage persists from three pin-point sinuses.
10	M	56	Pain	Incision and drainage, and biopsy	Yes	None	Left at own request against advice; followed for 7 4/12 years; no recurrence of disease in sternum; bedridden past 3 years.
11	M	46	Pain	Curettage	Yes	Spine	Still hospitalized; has open granulating wound over manubrium, with purulent drainage.
12	F	1½	Swelling	None	No	Finger Spine Lungs	Still hospitalized; sinuses are healed.

In 25 per cent of the cases, the tuberculosis of the sternum became arrested spontaneously and the sinuses healed. In the remaining 75 per cent, a variety of operative procedures were performed, such as aspiration, incision and drainage, curettage and the resection of sinuses. Since these operations were performed by different surgeons in different hospitals, accurate evaluation is difficult. Aspiration was performed in 3 cases, in two of which further operation was unnecessary; in the third, resection of sinuses was performed later. Herrick[1] also reported a patient in whom aspiration was performed and whose lesion healed under conservative treatment. In the other cases, incision and drainage were done at least four times,

and curettage at least twice. The operative end results were usually good, regardless of the procedure followed.

With the aid of social service, a follow-up was possible in all the cases discharged from the sanatorium. Two patients in this series (Cases 11 and 12) are still hospitalized, and a third (Case 7) died while in the sanatorium. Autopsy in this last case revealed tuberculosis of the sternum, ribs, pleura, pericardium, mediastinum and anterior chest wall. Of the 9 discharged patients, 2 (Cases 4 and 5) have died, one of pulmonary tuberculosis, and the other of arteriosclerosis. In neither was there recurrence of the disease in the sternum. A third patient (Case 2), a Chinese boy in ex-

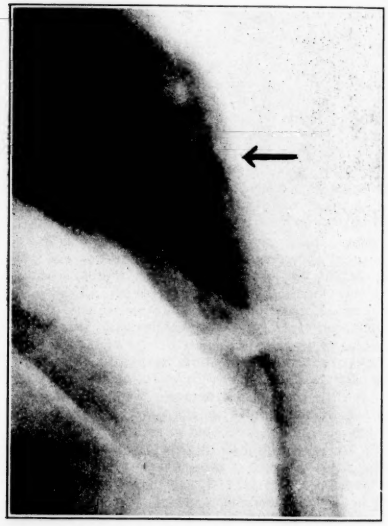

FIGURE 3. *Lateral View of Manubrium (Case 11). The outline is irregular, and there are many small rarefied areas within the bone.*

tremely poor condition, was taken by one of his parents to China and probably died en route.

Six cases were followed from ten months to eleven years and three months, with an average of over six years. In only one patient (Case 9), followed only ten months, does slight drainage persist. None of the other patients have had any recurrence of the disease in the sternum. All sinuses have remained healed, and there has been no swelling, pain or tenderness. One of the patients (Case 6), however, has far-advanced pul-

FIGURE 4. *Lateral View of Xiphoid Process (Case 10). Note the irregular contour and the areas of apparent bone destruction.*

monary tuberculosis, and another (Case 10), has been bedridden for three years because of a cerebral hemorrhage. In no fatal case in this series could tuberculosis of the sternum be regarded as a cause of death.

SUMMARY AND CONCLUSIONS

Twelve cases of tuberculosis of the sternum are reviewed. Sternal tuberculosis is almost invariably secondary to other demonstrable tuberculous foci. Painless swelling in the region of the sternum is the usual presenting symptom. The end results of conservative treatment are consistently good; radical surgery is apparently unnecessary.

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TOXIC EFFECTS IN MAN OF OVERDOSAGE WITH SODIUM SULFAPYRIDINE*

Report of a Case

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ALTHOUGH considerable study of the acute toxicity of sodium sulfapyridine in animals has been made by Marshall and Long,[1] little evidence concerning the effects of comparable dosage in human beings is available. Such information, of course, would not be voluntarily sought, but acute toxicity is likely to arise only through error in the administration of the drug. Such an error occurred at the Rhode Island Hospital in December, 1940, and provided us with information that we believe merits a brief report. Although similar experiences have undoubtedly been observed elsewhere, we have been unable to find in the literature any recorded case of similar overdosage and its effects.

Marshall and Long[1] observed that the intravenous administration of 0.5 gm. of sodium sulfapyridine per kilogram of body weight in dogs resulted in marked vomiting and severe convulsions; 2 out of 5 animals died. Blood levels of 53 to 64 mg. of free sulfapyridine per 100 cc. were attained one hour after the drug was given. Administration of 0.3 gm. per kilogram resulted in vomiting, tremor and convulsions, but the animals survived; blood levels of 36 to 37 mg. of the free drug per 100 cc. of blood were reached after one hour. At a dosage of 0.2 gm. per kilogram, muscular twitching and ataxia, with blood levels of 20 to 24 mg. of the free drug per 100 cc. of blood, were observed. These investigators found that rabbits experienced similar but much less marked symptoms on comparable dosage of the drug but had approximately the same blood levels. They observed that rabbits acetylated the drug rapidly, whereas dogs were unable to conjugate it. Since man also acetylates the drug, the toxicity in human beings should be more comparable to that observed in rabbits than in dogs. Kohn-Richards[2] reported similar experimental studies. He found that the intravenous injection of 1.0 gm. of sodium sulfapyridine per kilogram was uniformly fatal, if given alone. However, when pentobarbital-sodium was also given in adequate dosage, animals survived the intravenous injection of 1.2 gm. of sodium sulfapyridine per kilogram. Apparently, the pentobarbital mitigated the convulsive action of the sulfapyridine.

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CASE REPORT

A 26-year-old laborer was admitted to the Medical Service of the Rhode Island Hospital on November 12, 1940, complaining of epigastric pain and vomiting. He had had recurring episodes of epigastric pain, 1 or 2 hours after meals, for about 12 years, and a duodenal ulcer had been first demonstrated by x-ray 8 years previously. The most recent exacerbation began 3 or 4 months before admission, and was characterized by pain, nausea and morning vomiting. In December, 1939, the patient entered the hospital for repair of an incisional hernia. Following this he developed a postoperative pneumonia and was treated with sulfapyridine by mouth in adequate dosage for 4 days. Except for moderate vomiting, no toxic symptoms were evident, and recovery was prompt. His family history was of interest in that both his father and brother had suffered from duodenal ulcers for years.

Physical examination was negative except for moderate epigastric tenderness. The weight at entry was 140 pounds (63 kg.). Laboratory studies revealed normal blood counts and repeatedly normal urines. The blood Wassermann and Hinton reactions were negative. X-ray examination of the gastrointestinal tract again showed the presence of a duodenal ulcer. During the first several days in the hospital, the patient did fairly well but continued to have mild epigastric pain. Since he desired permanent relief from his recurrent disability, a subtotal gastrectomy was decided on and performed on November 26.

On November 27, the patient began to cough, raising greenish-yellow tenacious sputum. The temperature rose in the afternoon to 103.2°F., and the respirations to 40. On the following morning, examination revealed increased breath sounds at the left base and rales at both bases. A roentgenogram showed considerable haziness at the left base. It was believed that the patient had bronchopneumonia, and intravenous sodium sulfapyridine was ordered — 4 gm. immediately and 2 gm. in the late evening. The intern in charge ordered, and believed he was using, a 1 per cent solution of sodium sulfapyridine and calculated the amount of fluid for intravenous administration accordingly. The drug was given on November 28 at 1:30 and 11:00 p.m. The following morning it was discovered that a 5 per cent solution of sodium sulfapyridine had been used instead of a 1 per cent solution. Therefore, the amount of drug administered by vein had been a total of 30 gm. in about 10 hours — 20 gm. (0.32 gm. per kilogram) at 1:30 p.m. and 10 gm. (0.16 gm. per kilogram) at 11:00 p.m.

About 15 minutes after the administration of the 20-gm. dose, the nurse noted that the patient was extremely

restless; ⅙ gr. and, 30 minutes later, ⅛ gr. of morphine were given subcutaneously, with very little effect. During the afternoon he continued to be very restless and uncooperative, whereas he ordinarily behaved well. In the late afternoon he began to vomit and hiccough, and he continued to vomit during the next 36 hours. At 9:00 p.m., 2 gr. of luminal-sodium was given intramuscularly, with no effect. At 11:00 p.m., the mistake in the strength of the solution not having been discovered, 10 gm. of sodium sulfapyridine was given intravenously.

On November 29, restlessness became even more marked, and at 2:00 a.m. another 2 gr. of luminal-sodium was given intramuscularly. At 4:00 a.m., 1 cc. of paraldehyde was given intravenously in an attempt to quiet the patient, but was absolutely without effect. At 7:00 a.m., 30 cc. of paraldehyde was given by rectum, with slight sedative effect. At no time were convulsions or gross muscular twitching observed, and the patient was always clear mentally. He stated that he could not lie still. At 7:30 a.m., it was noted that the urine was dark and smoky. Examination of this specimen showed it to contain innumerable red cells and acetyl sulfapyridine crystals. Since a sample of serum contained no hemoglobin, no acute hemolytic process was present. During the morning the error in dosage was discovered, and large amounts of intravenous fluids were started. During the next 24 hours, the patient received 6500 cc. of 5 per cent dextrose in distilled water, and 1000 cc. of 5 per cent dextrose in saline. The urine continued to be grossly bloody, but he voided 1560 cc.

On November 30, during the early morning hours, the patient began to feel better and slept intermittently. The vomiting had ceased, although he was still somewhat nauseated, and the restlessness had largely disappeared. During the 24 hours he received 2500 cc. of 5 per cent dextrose in distilled water and 1000 cc. of 5 per cent dextrose in saline. The urine output was 3100 cc. In the afternoon, the urine was no longer grossly bloody, although microscopic blood was still present. On December 1, the major complaint was lower abdominal pain, which was relieved by bladder irrigations of distilled water. It was thought that the discomfort was due to a chemical cystitis. This pain gradually subsided during the next few days.

On December 3, moderate jaundice was first noted, and the patient complained of some right upper-quadrant pain. The lungs were clear. After the administration of sulfapyridine, the temperature had not risen over 101°F., and over the course of several days it gradually fell to normal. Because of the jaundice, he was given intravenously 2000 cc. of 10 per cent dextrose in distilled water daily for the next 5 days.

The jaundice gradually subsided and was not visible on December 10. No leukopenia, significant fall in the number of granulocytes or drop in hemoglobin occurred. Improvement was steady, and the patient was discharged on December 17, feeling quite well.

On February 28, 1941, he was seen by one of us (F. B. C.) and reported that he was feeling fairly well but had not yet regained full strength. Physical examination was negative. No jaundice was evident, and the liver edge could not be felt. A complete blood examination was entirely negative. A urine specimen had a specific gravity of 1.025, and was negative for sugar and albumin. Microscopic examination of the sediment, after centrifuging, revealed no casts or red cells. Two to four white blood cells per high-power field were present, probably the result of a low-grade bladder infection following the previous bladder irrigations. Chemical examination of a portion of the urine specimen for sulfapyridine was negative. The blood urea nitrogen was 13 mg. per 100 cc.

In Figure 1 some of the laboratory findings are charted. Unfortunately, no blood was taken for drug determination until 10 hours after the second intravenous dose. At that time there was still 20.7 mg. of free and 29.0 mg. of total sulfapyridine per 100 cc. of blood. The method employed

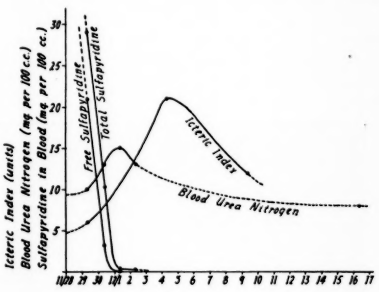

FIGURE 1.

was that of Bratton and Marshall,[3] using a 1:75 dilution of the blood, after standardization for sulfapyridine on the Cenco photelometer. The free drug had been excreted 57 hours after the last administration, although traces of acetyl sulfapyridine were still present 81 hours after the second dose.

SUMMARY

The patient in this case, suffering from postoperative pneumonia, received, through an error, 30 gm. of sodium sulfapyridine intravenously in a ten-hour period. He survived probably because of his youth, good kidney function and the prompt administration of large amounts of intravenous fluids. Convulsions, muscular twitching and anuria were not observed, but marked restlessness and irritability, gross hematuria and jaundice were strikingly evident.

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GUMMA OF THE FRONTAL BONE

Report of a Case

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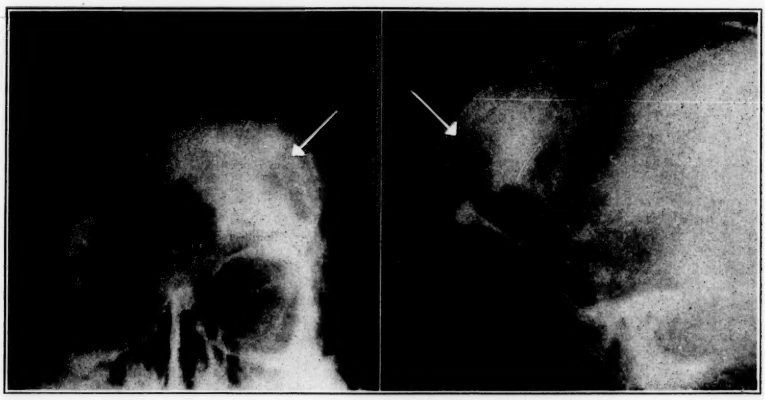
FEW general practitioners who have occasion to treat late syphilis have an opportunity to watch a definite lesion clear up dramatically under treatment. Frequently the wisdom of intensively treating such cases is questionable, in view of reactions. The following case of gumma of the frontal bone completely resolved under antisyphilitic therapy that could by no means be called intensive. Furthermore, it illustrates that the titer of a serologic test for syphilis may remain exactly the same in spite of a dramatic clinical result.

CASE REPORT

G. D., a gas-station attendant, had first consulted a physician on December 25, 1937, because of pain and swelling in the right forehead after a glancing blow several days previously. Hot compresses were advised, and 24 hours later the area was incised. According to the patient, "quite a lot of pus came." The lesion was dressed daily, but evidently became progressively worse.

I was first consulted on February 4, 1938. At that time, a draining, ulcerated lesion about the size of a half dollar was found just above the right eye. The upper right lid was edematous, and the eye was completely closed. Bare bone could be detected at the base of the ulcer. The skin edges were widely undermined to the mid-forehead, beyond the hairline, to the zygomatic arch and into the upper lid. The temperature, pulse and respirations were normal. Examination of the urine was negative. Hospitalization was advised and promptly refused. A blood serologic test, culture and biopsy, suggested as an alternative, also met with refusal. The patient insisted that all he wanted was "some salve and something for the pain." Believing that he might possibly feel differently later, I applied zinc peroxide paste to the lesion; codeine was prescribed for the pain, and the patient was told to return on the next day. However, he did not return until March 4.



A B

FIGURE 1. *X-Ray Films Taken March 4, 1938. A is the anteroposterior view; and* B, *the lateral.*

In the meantime, the pathologic process had gone from bad to worse. Practically the entire right forehead had become ulcerated, and the pain was intense. The temperature, pulse and respirations were still normal. Although the patient continued to refuse hospitalization, he agreed to permit certain procedures. X-ray films of the right frontal region and blood for a serologic test for syphilis were then taken. Smears of the lesion were negative for tubercle bacilli. The patient was placed on 15 gr. of potassium iodide empirically, the lesion was cleansed, and a dry sterile dressing was applied. The test for syphilis was reported as positive in a titer greater than 1:10. The x-ray films (Fig. 1) were reported as follows by Dr. James W. Walton, of the Horton Memorial Hospital:

Radiographic examination reveals an area of disease in the right frontal bone extending down to the zygomaticofrontal suture, backward almost to the frontoparietal suture and medially almost to the mid-line. The lesion is approximately 7.5 cm. in diameter, with densely sclerosed edges and an area of rarefaction in the center measuring at least 2.5 cm. in diameter. This area is very circumscribed and has very densely sclerosed edges, and because of its location, could be a gumma. If a definite history of injury some time ago can be obtained, chronic osteomyelitis must be considered, but there is more sclerosis than is usually seen in this condition.

The dose of potassium iodide was immediately increased to 30 gr., and protiodide of mercury was administered in doses of ¼ gr. three times daily. Within 48 hours, the pain was relieved. On March 9, the patient was started on small doses (0.2 gm.) of Bismarsen. Mapharsen was instituted on March 24.

The x-ray report on April 18 was as follows:

> Radiographic re-check of the right frontal bone shows very extensive resolution of the area of sclerosis with central destruction — apparently a gumma — previously reported. The smaller areas previously reported also show considerable resolution.

The clinical appearance of the lesion had also been markedly changed. The edema of the right upper lid had disappeared, the drainage had ceased, and granulation tissue had appeared. Most important of all, the "soreness" had entirely disappeared. Antisyphilitic therapy was continued, with a shift to 0.2-gm. doses of Bismarsen on June 6, but only dry sterile dressings were applied to the wound.

The last x-ray films (Fig. 2) were taken on June 17, and were reported as follows:

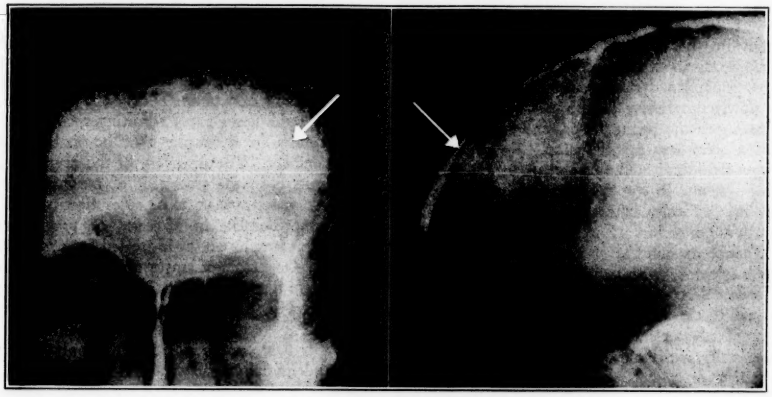
> Radiographic re-check of the right frontal bone shows complete resolution of the area referred to in previous examinations (Fig. 1). There is moderate bone sclerosis in this area.

Clinically, the lesion had entirely healed with the exception of a small area about 3 mm. in diameter. This cleared up about 2 weeks later.

Treatment was continued until July 30, but during the entire course of the disease the patient received only ten injections of Mapharsen and eleven of Bismarsen. Repeated serologic tests for syphilis remained positive, with a titer greater than 1:10.

The patient was seen on March 1, 1940, for another complaint, and at that time, with the exception of a barely noticeable amount of puckering, nothing remained of the original lesion.

Although not many cases of gumma of the frontal bone have been reported, the lesion is not generally considered rare. Most patients seem to do well, but complications occur in the underlying structures, and deaths have been reported. In the diagnosis, the most important feature is to think of the possibility of and to take a specimen for a serologic test for syphilis in all open lesions. This case is of further interest in that the therapy was not too intensive because the patient would not co-operate, the blood titer remained unchanged, and yet the lesion responded dramatically.



A B

FIGURE 2. *X-Ray Films Taken June 17, 1938.*
A *is the anteroposterior view; and* B, *the lateral.*

SUMMARY

A case of gumma of the frontal bone is presented, and the importance of serologic tests in all such open lesions is stressed. Antisyphilitic therapy brought about complete resolution of the lesion, even though the serologic titer remained exactly the same.

MEDICAL PROGRESS

NEUROLOGY

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VITAMIN E AND CERTAIN DISEASES OF THE NERVOUS AND MUSCULAR SYSTEMS

TWO diseases have come into prominence during the last two years because of possible successful treatment by vitamins, and especially by vitamin E: namely, amyotrophic lateral sclerosis and progressive muscular dystrophy.

Before the effect of treatment is discussed, a few words about diagnosis are in order. Progressive muscular dystrophy is generally considered a slowly progressive disease in which muscle-fiber wasting is the prime factor, and replacement by fat a secondary manifestation. No causative lesions are found in the central or peripheral nervous system. In the typical advanced case, there is little difficulty in making a diagnosis; in the early stages and in atypical cases, diagnosis is often in doubt for months or years. Amyotrophic lateral sclerosis, when conforming to the original Charcot description, is a disease of the spinal cord in which the latter shows, anatomically, degeneration of the anterior-horn cells and pyramidal tracts bilaterally, with no evidence of inflammation, compression or vascular disturbance. Clinically, the patient shows weakness, with atrophy of the muscles, usually beginning in the hands, and spasticity, usually beginning in the legs; the two processes relentlessly extend in intensity and in parts involved, and end in bulbar palsy.

Amyotrophic lateral sclerosis in its early stages and even later also simulates a number of other conditions, so that most neurologists advisedly make the diagnosis of "amyotrophic lateral sclerosis syndrome." Later developments show that a large number of these patients do not run the course of the typical Charcot description. Rubenstein[1] has recently emphasized this point: of 8 cases studied, only 4 were typical; the other 4 afforded evidence that somatic disease caused a clinical picture similar to that of the disease under consideration.

The difficulties in diagnosis must be kept constantly in mind before one accepts at face value the results of treatment in these two diseases. And yet it is fair to say that when the clinical picture is such that either diagnosis has been seriously entertained, the outlook for recovery is not good, and any agent that will arrest the process should therefore be welcome, whatever the exact diagnosis.

In 1939, at the International Neurological Congress at Copenhagen, a paper by Einarson and Ringsted[2] on vitamin E stimulated interest. They observed atrophy and spinal-cord degeneration in rats as a result of vitamin E deficiency. In 1940, Bicknell[3] published a paper reporting such encouraging results in dystrophy that he makes this bold statement, "The discovery of the importance of vitamin E in the treatment of muscular and nervous diseases appears to be revolutionary." He claims improvement in 12 cases of progressive muscular dystrophy out of 13 treated for six weeks or more. Of 4 cases of amyotrophic lateral sclerosis, 2 were improved, and 2 died with bulbar paralysis. His treatment was 15 gm. of dried whole-wheat germ twice daily by mouth. His case reports are meager, frequently only a few lines, and improvement was often admittedly dependent on report rather than personal evidence. On the basis of evidence given, it is difficult for one to reach the optimistic conclusions quoted above. Stone[4] is also encouraged by treatment of pseudohypertrophic muscular dystrophy and of myatonia congenita. Wechsler[5, 6] undoubtedly is chiefly responsible for stimulating interest in vitamin E in the United States. In his later paper, he analyzes 20 of his 30 cases of amyotrophic lateral sclerosis. He admits a difficulty in diagnosis but believes that vitamin E is especially successful in the degenerative type. He used alpha tocopherol acetate by mouth, up to 50 mg. daily, and intramuscular injections of this drug in oil; he also gave 2 teaspoonfuls of wheat-germ oil by mouth. Vitamin B complex and a vitamin-rich diet were also given. Two patients recovered, 4 showed marked improvement, and 6 improved somewhat.

A number of other papers on this subject have been published during the past year, some strongly in favor, others giving negative results of treatment. Papers written from four large clinics—Cornell, Columbia, Mayo and Harvard—uni-

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formly show poor therapeutic results. Denker and Scheinman,[7] using even larger doses of vitamin E than those recommended by Wechsler, assert, on the basis of 15 patients, that "no therapeutic results of any value were observed." Ferrebee et al.[8] state that "vitamin E and vitamin B_6 preparations, given in large amounts, failed to influence the course of either amyotrophic lateral sclerosis or muscular dystrophy in a series of patients followed for a period of two to twelve months." Workers at the Mayo Clinic[9] and at the Neurological Unit of the Boston City Hospital[10] are likewise unimpressed.

At a meeting of the Boston Society of Psychiatry and Neurology in April, reports were made from the Boston City and Massachusetts General hospitals, and the conclusions reached and the discussion were pessimistic. However, in chronic diseases, with the diagnostic difficulties mentioned earlier, one should not judge too quickly a therapy that has the support of men of the standing of Wechsler.

The best results have been obtained in the treatment of dystrophy in children; the worst results have been in cases of bulbar palsy. Another year should determine the value of this form of treatment.

Basilar Anomalies and the Arnold–Chiari Malformation

For many years, malformations of the occiput, atlas and axis have been recognized as interesting anomalies. Knowledge of the displacement of medulla, cerebellum and spinal cord, commonly known as the "Arnold–Chiari malformation," goes back to 1894 and 1895.

Recently, there have been attempts to establish a relation between these anomalies, one of bony development, the other of the central nervous system. Although the two conditions occur independently of each other, there appears to be a developmental relation. The symptomatology is similar enough to include both conditions in comparative discussion. To be thoroughly inclusive in a clinical differentiation at this level, one should also consider syringomyelia and high cervical-cord tumor.

An extremely lucid and well-illustrated paper on the bony anomalies of this region is that of List.[11] He explains the anomalies on a basis of abnormal fetal development and incorrect ossification, with subsequent modification by rickets, weight bearing and so forth. He recognizes in his cases four types of deformity: malformation of the occipital foramen and basilar impression (platybasia); fusion of the atlas with the occiput and malformation of the atlas; fusion of other cervical vertebras and malformation of these vertebras; and abnormal position of the axis in relation to the occiput and atlas. These anomalies may be considered essentially benign, but with continued growth and under stress, neurologic symptoms may arise. The chief interest concerns platybasia, in which the basiocciput is thinned and mushroomed upward by the atlas, and the foramen magnum is narrowed. The medulla resting on this floor is thus compressed anteriorly and constricted in its passage through the narrowed foramen magnum. The neurologic picture is naturally one of medullary compression, and when the fluid pathways become obstructed, of superadded hydrocephalus. If in the advance of the process, dislocation of the axis on the atlas occurs, upper cervical-cord symptomatology is to be expected.

The Arnold–Chiari deformity concerns the nervous system. The medulla and cerebellum are displaced downward through an enlarged foramen magnum into the cervical canal. In the case reported by Penfield and Coburn,[12] the cerebellum extended to the third cervical vertebra. Such a displacement leads to medullary jamming in the foramen magnum, with extreme traction on the lowest cranial-nerve roots and with cerebellar symptoms, and additional symptoms of increased intracranial pressure. The mechanism by which this downward herniation of the brain through the foramen magnum occurs is not always clear, but in Penfield's case it was satisfactorily explained as follows: in childhood, the patient had been operated on for a mid-dorsal meningocele; at autopsy, the dura and consequently the spinal cord and nerve roots were firmly adherent at the point of operation. It seemed apparent that this attachment prevented the normal ascent of the cord in the spinal canal with growth, and consequently the upper portions of spinal cord, medulla and cerebellum were slowly drawn down. This mechanism is probably not the only possibility in explaining the downward displacement, for in some cases there is no meningocele. Adams and his associates[13] have studied a case of this type, without evidence of meningocele. An operative decompression so completely relieved the symptoms that the patient returned to work.

Although points of clinical differentiation are made between platybasia and the Arnold–Chiari malformation, both conditions produce slow pressure on the medulla, cerebellum and low cranial nerves, and both conditions must be considered in lesions that indicate an abnormality near the foramen magnum. Furthermore they must be differen-

tiated from high cervical-cord tumor and syringobulbia. Perhaps the most valuable accessory examination is that by x-ray. In bony abnormalities with medullary compression, the foramen magnum is narrowed; in the Arnold-Chiari malformation, it is enlarged. Chamberlain[14] gives details of x-ray examination, which should include a frontovertex projection to show the foramen magnum, and a lateral view in which a line drawn from the posterior rim of the foramen to the hard palate passes above the odontoid process, or below it if there is basilar impression. Gustafson and Oldberg[15] present 5 cases in which operation was performed for platybasia, and strongly recommend decompression of the foramen magnum.

Epilepsy

During the last few years, intensive work on epilepsy has been yielding more and more to the understanding and treatment of convulsions. Much of this work stems directly or indirectly from the lifelong persistent studies of Dr. William G. Lennox and his associates at the Boston City Hospital. For years, their groundwork studies were apparently negative, in the sense that nothing of value could be passed on to others. That prolonged study of brain circulation through a window gave them much information is certain. The use of electroencephalography has placed in their hands a tool of great value and has led to a more definite conception of epilepsy; for example, it has been learned that convulsions are due to abnormal electrical discharge from the brain and that electrical cerebral dysrhythmia is a factor in such seizures. The addition of another drug — Dilantin — to the arsenal of useful anticonvulsants is another contribution of first magnitude from this group.

Dr. Lennox has always had an interest in the social implications of epilepsy. A paper by Lennox, Gibbs and Gibbs[16] discusses inheritance in epilepsy. Using the electroencephalogram, which they have come to consider the most reliable index of latent as well as active epilepsy, they report family studies that show a marked preponderance of dysrhythmia — and therefore supposed latent epilepsy — in the relatives of epileptic patients. The number of epileptic patients in the community is large, and the authors find that persons with a "predisposition to epilepsy form about 12 per cent of the population."

Appalled by the number of epileptic patients, and even more by the social ostracism enforced on them, Dr. Lennox some years ago formed the Laymen's League against Epilepsy, to combat ignorance and prejudice about convulsive disorders and to encourage research in this field. He[17] has just published a book for laymen wherein he describes, in nonmedical language, what is known and what is not known about epilepsy and migraine. This book should, in my opinion, be recommended to every epileptic patient or his family, for it describes authoritatively what every doctor should tell his patient about the many accessory causes of attacks. Especially important, it should deter an intelligent patient or his family from the costly and inhuman practices now as always so commonly in vogue — "medical shopping."

From the surgical point of view, Penfield has shown an ever-increasing interest in epilepsy. His earlier work with Foerster led him to further studies of focal irritability of the brain as the cause of jacksonian and generalized seizures. Two recent papers by him and his associates[18–19] at the Montreal Neurological Institute may be considered together. It is well known that large scars of the cortex not infrequently cause convulsions, but it is still a debated point in what manner they do so, and especially why epilepsy comes on months or years after accident or infection. Penfield's chief interest is the small focal lesion, its excision and its microscopic examination. He considers the formation of focal cortical scars in the 8 children described to be due to three causes: ischemia at birth; vascular occlusions in early prenatal or postnatal life; and infantile meningitis. Although individual lesions may be small, many such focal lesions may lead in time to asymmetrical brain development and gross hemispheric displacement. The epileptogenic zones are outlined by electric stimulation, and excised. The histology is of especial interest; small areas devoid of nerve tissue are surrounded by glial scar tissue that shows increased vascularization. Most significant of all is the presence in this zone of glia-cell swelling and phagocytosis. The hypothesis offered is therefore that in this zone lying on the edge of an area of focal destruction is scar tissue that is constantly changing, probably as a result of alternating vascular dilatation and constriction, and further that this is the seat of abnormal electrical responses and of epilepsy.

As another diagnostic aid in determining the localization of a suspected corticomeningeal scar, Olivecrona[20] has used subdural pneumography. The patient had developed fits of no definite pattern following an accident to her left forehead many years before. Neither neurologic nor x-ray examination, including encephalography, revealed the location of the supposed cortical scar. Air was therefore injected into the subdural space through

bilateral frontal trephine openings, the cerebrospinal-fluid pressure being lowered by lumbar puncture to facilitate the filling of the subdural space. An x-ray film showed clearly a tentlike projection of tissue, which prevented air filling in the left postfrontal region. This was subsequently found to be scar tissue and was removed at operation, with cessation of attacks.

It is of course well known that convulsions are a frequent accompaniment of brain tumor. That epilepsy may be the first symptom of tumor is likewise recognized. But it will come as a surprise to many that, in two types of brain tumor, — astrocytoma and meningioma, — seizures occur as the first symptom in 60 per cent and 62 per cent respectively. The figures are from the Montreal Neurological Institute.[21] It is interesting to note that these types of tumor are the two that are most frequently operable; furthermore, the tumors are encapsulated and near the surface of the brain. The obvious deduction from this paper is that a patient with late epilepsy must be considered a "brain-tumor suspect" and every effort made to confirm the diagnosis.

Although uncommon in the United States, cysticercosis as a cause of epilepsy should not be forgotten, particularly in view of the accuracy of diagnosis. The question should always be considered in any patient returning from the Orient. Dixon and Smithers[22] speak of epilepsy, generalized or jacksonian, as frequently occurring in this disease. The brain cysts may or may not be calcified. The diagnosis is made presumptive when large numbers of calcified organisms in the skeletal muscles are revealed either by palpation or by x-ray study.

Ray[23] has recently published a case report of especial interest because of the satisfactory outcome following surgery. The patient evidently became infected in India; the diagnosis was correctly made in 1936 in England on the basis of convulsions and the demonstration of calcified cysticerci in the muscles. Presumably because brain metastasis is often multiple, surgery was not offered at that time. Soon after, Ray successfully removed a solitary cyst from the parietal cortex and confirmed the diagnosis histologically. The patient was said to be well and working, four years after operation.

Frontal Association Areas and Operations on Them

Because the frontal lobes are phylogenetically new and well developed in man as compared with any lower animal species, it is reasonable that they should have been considered the seat of intellect. That this is only partially true is becoming evident, as studies on apes and most significantly on man himself are beginning to reveal. Since operative procedures on this region are now designed with increasing boldness, it is well to consider what is already known.

It is necessary to distinguish the anatomic frontal lobe from the frontal association areas. The posterior portion of the frontal lobe is bound up with motor function, posture, speech and eye movements, and the anterior portion, which is histologically different, has no direct control over these functions. The latter areas, which are so well developed in man, are the regions under consideration: the frontal association areas.

Physiologic evidence of function of these areas, as abstracted from Fulton's[24] work, is as yet not great and not too certain. He states:

> The frontal areas are inexcitable to all forms of electrical stimulation and their primary ablation has little if any effect upon reflexes or posture of the extremities in any primate form including man. . . . Unilateral ablation . . . causes no obvious behavioristic disturbance in monkey, chimpanzee or man; but their *bilateral* destruction leads to a conspicuous syndrome characterized in animals by restlessness, distractibility and failure of immediate memory.

He cites Jacobsen's experiments with apes; these indicate that bilateral ablation appears to show that recently acquired experience could not be assimilated and utilized in problems that were readily solved by the same animals before operation or after unilateral frontal ablation. Jacobsen's experiments with conditioned reflexes were most interesting. When balked, the normal animal became frustrated to a degree approaching neurosis. After bilateral frontal ablation, the same mistakes called forth little or no emotional response. The animal was restless and distractible but presented the "fatuous equanimity of spirit which one encounters in a good-natured drunkard."

Because the frontal association areas are preeminently well developed in man, it is probable that their function will be revealed by studies on man. There is general unanimity of opinion that unilateral ablation or destruction fails to show clinical evidence; neither abnormal performance nor lack of it can be recognized by present methods. Although a tumor of one frontal lobe may be accompanied by personality changes, close analysis invariably discloses the certainty that no abnormality existed until the tumor had expanded sufficiently to implicate the other frontal lobe by pressure or by invasion of the corpus callosum. I have recently had a clear-cut demonstration of this point in a nineteen-year-old girl who at fifteen years of age had had a convulsion. X-ray ex-

amination of the skull at that time showed a definite deposit of calcium in the tip of the right frontal lobe. Since no other symptoms and no further attacks of epilepsy appeared, the patient continued her studies, was admitted to college, and was considered a normal girl in every way. Only when headache supervened five years later, with evidence of increased intracranial pressure, did her intellectual output suffer, together with an alteration of personality of which distractibility, facetiousness and punning were outstanding. At operation, Dr. W. Jason Mixter was obliged to resect the right frontal lobe up to the premotor area because of an invasive tumor, probably an astrocytoma.

Almost every physician will probably recall at least one patient with a small lesion of one frontal lobe, whether from tumor, trauma or abscess, that gave no hint of its presence until sufficiently large to alter the function of both frontal lobes. Jefferson,[25] on the basis of 8 unilateral frontal lobectomies, states: "Those who showed no mental alteration before the operation were unaffected by partial removal of the anatomical frontal lobe . . . those who had mental symptoms [because bilateral function was presumed to be affected] were much better after the lobe had been excised." Nor did Jefferson and other authors find evidence for right or left frontal-lobe dominance if the lesion was confined to the prefrontal region.

In a discussion of frontal-lobe symptoms, bilateral involvement of the frontal association areas is therefore implied. To most observers, the character changes as represented by the general paretic come first to mind; others remember the personality traits of Phineas Gage, whose frontal lobes were largely destroyed by a crowbar.[26] The placard accompanying the skull and bar in the Warren Museum reads, "His disposition was noted to change but in minor ways: he became fitful and vacillating, profane and obstinate, which was different from what he had been before the accident, but no other deviation was noted."

But neither of these examples can safely be depended on as evidence that personality traits reside in the frontal lobes. Nor can one say that the frontal lobes act as a brake on the restlessness, the emotional instability, the joking and the obscenity of such a patient. Brickner[27–29] has made what is probably the first and most extensive study of an appropriate case, a man in whom Dandy removed both frontal association areas because of a tumor (meningioma) confined to this region. The objective characteristics of this man, which continued unchanged from the operation in 1930 to the last report in 1939, were not greatly different from those of Phineas Gage. The patient was emotionally unstable, a braggart, a wife-baiter and a silly punster, and he was often vulgar and obscene. His mental processes were not deficient, but he showed intellectual inertia. His wife stated that his postoperative traits were not different from what they had been before, but that they were intensified. After thorough psychologic tests, Brickner concludes that this array of unproductive traits is the result of a "diminution in the amount of synthesis, which places a limit upon the degree of attainable complexity of thought."

Hebb and Penfield[30] report on bilateral frontal lobectomy in a man presenting post-traumatic epilepsy and a personality change to the extent that he had "become a behavior problem — irresponsible, childishly stubborn, restless and forgetful." Following the operation, convulsions were reduced to a minimum, intelligence improved, as shown by specific tests, and behavior was now socially acceptable. The authors are unwilling to commit themselves about the extent to which the frontal association areas influenced the behavior of this man: "It may be that no laboratory study will be adequate to reveal whatever defects follow frontal injury in man because of insufficient control of environmental factors and the difficulty of obtaining a good premorbid rating of ability."

It therefore seems possible to produce certain changes of behavior and disturbance of intellectual balance by partial destruction of the frontal lobes, and also to bring about improvement in behavior and intellect by ablation of the same areas. This brings us to the crucial experiment, usually only possible in the physiologic laboratory, but now practiced on man for therapeutic purposes, that is, bilateral frontal lobotomy on the normal cortex. In this country, Freeman and Watts[31] have been the pioneers in this operation, which consists in cutting the nerve-fiber connections of the frontal association areas: "The white matter in each frontal lobe is cut just anterior to the tip of the ventricle in the plane of the coronal suture." This operation on man may be considered to be based on the observations of Jacobsen on apes, mentioned above, and is used for its stabilizing effect on cases of agitated depression.

Excerpts of three stages of the effects of the operation will give an impression of the results to be expected:

> The patients can converse quite rationally during the operation upon either the right or the left side of the brain, but often as soon as the first incision is made in the frontal lobe on the opposite side, there is immediate abolition of anxiety and nervous tension; the pulse and blood pressure fall within a few minutes,

the skin of the extremities becomes warm and flushed, and there is considerable sweating. As the incision into the white matter is made more extensive, the patient becomes disoriented, and with the final incision, upward or downward, becomes drowsy or goes into stupor from which he is roused with difficulty and answers in monosyllables.

During the following two or three days or longer, there is vesical incontinence, and the sluggish state persists. Neurologic signs other than these are usually absent. The physical condition remains good. The patients are often restless and try to get out of bed, and upon questioning are found to be completely disoriented. These patients present a placidity and indifference that forms a striking contrast to their previous apprehensive state.

When examination is carried out a month after operation, it is found that there is a certain inertia present. The patient responds courteously and accurately, but volunteers little. The relatives state that the patient spends most of his time sitting in a chair, not reading or playing games; apparently perfectly at ease, but merely unoccupied. . . . The patients make plans for tomorrow, but somehow, tomorrow never comes. They do enough for today, and then stop. On the other hand, if given a task of more or less repetitive character, they will often continue more or less automatically, beyond the limits of normal patience.

As an antidote to the distressing symptoms presented by a patient who is agitated and depressed, the remote effects of frontal lobotomy as above quoted are very welcome both to the patient and to his relations. The operation restores him to society, but not to competitive occupation. This fortunate outcome has been brought about in a patient known to me whose case was recently reported by Mixter and Tillotson.[32] The patient had remained unchanged for seven years in an institution, but for two years since operation has lived comfortably at home.

There is no clear answer to the question, What is the function of the prefrontal lobes or the frontal association areas? Brickner believes that these areas "synthesize" sensory impressions; Freeman and Watts believe that "they assemble the available data, synthesize them, plan a course of action with the idea in mind, and, equipped with energy of response and with appropriate affective tone, project the individual into the future, direct him toward his goal — and criticize his shortcomings." It also seems probable, as intimated by Hebb and Penfield, that these areas exert a control over psychologic processes that varies with the patient's previous intellectual and emotional life and the social environment in which he lives.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 27381

PRESENTATION OF CASE

A fifty-seven-year-old Italian woman entered the hospital complaining of vomiting of two weeks' duration. Because of the patient's condition, the history was obtained from her husband.

Seven years before admission, the patient visited her physician, complaining of pruritus, weakness and restlessness. A diagnosis of diabetes was made, and she was put on a diet without insulin.

She carried on until six months before admission, when for unstated reasons she saw another physician. He found that the urine contained a large quantity of sugar, boiled solid with albumin, and was full of red cells and casts. At this time, an oculist noted that the fundi showed "a combination of diabetic and albuminuric retinitis." Protamine insulin was now used in doses of 40 units twice a day. Three months later, the patient developed what appeared to be bronchitis, with a chronic cough and white sputum, began to lose weight rather rapidly, and suffered from weakness, headaches, dizziness, dyspnea and ankle edema. The symptoms progressed, and two weeks before admission anorexia and vomiting appeared and she became drowsy and listless. Her physician heard wheezes throughout her chest and recorded a blood pressure of 160 systolic, 90 diastolic. Digitalis was given, but since the vomiting grew worse, it was discontinued.

In the preceding few days, the family had noticed that the patient's speech and behavior were peculiar. At the time of admission, she was nearly blind, had lost 60 pounds in the previous six months, and had complained of frequency and a nocturia of once a night for some time.

At no time had there been pain, orthopnea, hemoptysis, hematuria, gravel, chills, fever, convulsions or localized weakness. Vomiting had ceased five days before entry.

The past and family histories were irrelevant.

On examination, the patient was in no acute distress, but irrational and very unco-operative. The ears, nose and throat were normal; the fundi were not seen. The heart was markedly enlarged to the left, with a gallop rhythm and an apical systolic murmur; the blood pressure was 210 systolic, 110 diastolic. Moist rales were heard at the lung bases. The liver was palpable two fingerbreadths below the costal margin, the abdomen being otherwise normal. Examination of the nervous system was negative, so far as it could be studied.

The temperature was 100.5°F., the pulse 120, and the respirations 25.

The urine ran a specific gravity between 1.008 and 1.015, with a ++++ test for albumin. The blood showed a red-cell count of 4,000,000 with 13.5 gm. of hemoglobin (photoelectric-cell technic), and a white-cell count of 6500. The nonprotein nitrogen of the blood serum was 38 mg. per 100 cc., the sugar 151, the protein 6.4 gm. per 100 cc.; the chlorides 99.8 and the carbon dioxide combining power 25.9 milliequiv. per liter. The stools were guaiac negative.

An x-ray film of the chest showed the heart to be enlarged in the region of the left ventricle. The lung fields were clear, and the aorta was not remarkable.

With an intravenous pyelogram, the size of the kidneys was in the upper limits of normal. No unusual areas of calcification were seen in the region of the kidneys, but multiple areas of calcification were present in the left side of the pelvis (probably phleboliths). Only traces of dye were visible in the kidney pelves, incompletely outlining them over a course of sixty minutes. Nothing could be said about the shape of the kidney pelves.

The patient was digitalized and given 40 units of protamine insulin daily, the urine remaining sugar free. There was a general improvement for a short time, but she remained disorientated, irrational and sometimes unruly. On the sixth hospital day, the nonprotein nitrogen was 40 and the sugar 140 mg. per 100 cc.; the carbon dioxide combining power was 20.8 milliequiv. per liter. The following day, a flaccid paralysis of the right arm and leg accompanied by aphasia suddenly developed and she was unable to take nourishment. The patient then became comatose, responding only slightly to painful stimuli.

Ten days after admission, tubular breathing and coarse rales were present in the right lower lobe, the temperature rose to 105°F., and the patient vomited occasionally.

Death occurred the next day, the temperature rising terminally to 108°F.

DIFFERENTIAL DIAGNOSIS

DR. JOHN H. TALBOTT: This abstract describes the medical history of an Italian housewife who

had suffered from diabetes mellitus for seven years, and from vomiting and mental disorientation for two weeks. The diabetes was presumably mild during the greater part of the period, for no insulin was necessary until six months before admission. The first evidence that something was wrong with the kidneys appeared during a routine examination for urine sugar. It was noted that the specimen boiled solid, probably because of the high albumin content. Examination subsequently revealed red blood cells and casts in the urinary sediment. Examination of the eye grounds showed diabetic and albuminuric retinitis. There is no mention of papilledema of the nerve head, and we can assume that there was not a significant increase in intracranial pressure.

The onset of the present illness may be dated by this examination. The need for 80 units of protamine insulin per day for a patient receiving none previously is significant. I have assumed from this observation that a complication of diabetes mellitus or some new malady was responsible. The story of a weight loss of 60 pounds confirms this assumption. Yet there were no clinical symptoms until three months before entry. The appearance of a chronic cough and white sputum suggested a pulmonary process, and the diagnosis of bronchitis was made. Symptoms of weakness, headache, vertigo, dyspnea and ankle edema then divert our attention from the lungs and center it on the cardiovascular-renal system.

The patient was admitted to the hospital because of vomiting and mental disorientation. I presume we can exclude a brain tumor, because the statement is made in the record that convulsions and localized weakness were looked for but not observed. Furthermore, if an expanding lesion of the brain were responsible for the cerebral symptoms, I should not expect vomiting to cease spontaneously. There is no further information about the eye grounds at the last admission, except that they were not visualized. No mention is made of the flexibility of the neck, and I assume it was not rigid. A gallop rhythm suggests that the heart was functioning at a disadvantage. The apical systolic murmur, enlargement of the heart by x-ray examination and the blood pressure of 210 systolic, 140 diastolic are indicative of further strain on the myocardium.

We have ample evidence of a renal dysfunction. The presence of large amounts of albumin was observed for at least six months. The maximum specific gravity of the urine was 1.015. It is not stated whether the maximum specific gravity was observed during a so-called "urine-concentration test," or whether this represented the maximum of several casual specimens. Recently, we have been helped by a new test for determining maximum urine specific gravity. The test needs less preparation than the other tests recommended and is probably more accurate. Without previous preparation, the patient is given 0.5 cc. of surgical pituitrin subcutaneously. Half-hourly urine collections are made for three hours, and the volume and specific gravity recorded. A normal person should concentrate to 1.020 during the test.

Turning again to the patient under consideration, it is reported that the nonprotein nitrogen was 38 mg. per 100 cc. and that the serum protein was 6.4 gm. per 100 cc. I believe that the patient was dehydrated on admission, and that this value if corrected for dehydration would be somewhat below normal. The serum chloride, carbon dioxide content and blood sugar were essentially normal. These concentrations do not permit us to make a diagnosis of diabetic acidosis and coma. X-ray studies showed normal lung fields. The intravenous pyelogram showed incomplete outlines of both kidneys, which were at the outer limits of normal in size. No abnormal calcification was seen.

During observation on the ward, the patient was digitalized, with some benefit. Paralysis of the right arm and right leg developed, however, and death followed, with a temperature of 108°F.

In summary, we can say that the patient had diabetes mellitus as well as hypertension. There was hypertrophy of the heart and cardiac decompensation. These diagnoses are given to us in the history.

The matters that we have to decide concern the precise nature of the renal disturbance and the pathogenesis of the cerebral symptoms. With the evidence given, we are entitled to be suspicious of a brain tumor, cerebral abscess, subdural hematoma and tuberculous meningitis. There is not sufficient evidence, however, to implicate any one of these specifically. If we rule out each of these cerebral conditions as being responsible for vomiting, and have no gastrointestinal studies to suggest a peptic ulcer or a neoplasm, it is reasonable to attribute the vomiting to chronic renal insufficiency. The remaining cerebral symptom to be explained, namely hemiplegia, can best be attributed to a vascular accident. Because of the frequent association of hypertension and hemiplegia, I should favor a cerebral hemorrhage.

The renal lesion is even more intriguing. I do not believe that this is a case of the usual variety of acute nephritis, nor am I concerned about the

diagnosis of nephrosis. It is true that most of the clinical findings could be explained by a diagnosis of chronic nephritis, but somehow it does not impress me as being the ordinary variety of chronic nephritis and uremia. This leaves us with but one choice. There is a particular type of kidney lesion observed frequently in patients of this age group suffering from diabetes mellitus and hypertension. The lesion is characteristically confined to the intercapillary spaces. I think it reasonable to believe that this patient had anatomic involvement of the intercapillary spaces, because from 15 to 30 per cent of well-studied autopsied cases of patients with diabetes mellitus and hypertension have such a renal disease.

Dr. Earle M. Chapman: You believe that the lesion shown at autopsy will probably be intercapillary glomerulitis, the type that Kimmelstiel and Wilson[1] reported from the Mallory Institute.

Dr. Talbott: On the law of probability, I should favor such a diagnosis.

Dr. Allen G. Brailey: Do you not think it is fair to assume that this goes back much longer than six months?

Dr. Talbott: I doubt if the patient had massive albuminuria for three years.

Dr. F. Dennette Adams: On the ward, we were at first unable to account for the mental picture. When the paralysis developed, we made a diagnosis of cerebral thrombosis rather than hemorrhage, and believed that the mental symptoms could be best explained on the basis of a progressive vascular lesion, which first affected a silent area. We expected that the brain at post mortem would show a large area of infarction.

Dr. Talbott: It might be of interest to mention the findings of one hypertensive patient examined in this department. The patient had symptoms typical of cerebral hemorrhage, an acute onset of paralysis, and at autopsy no evidence of acute hemorrhage or thrombosis was present. The patient had cerebral disease associated with malignant hypertension but no localized lesion.

Clinical Diagnoses

Diabetes mellitus.
Hypertension.
Hypertensive heart disease.
Nephrosclerosis.
Cerebral thrombosis.

Dr. Talbott's Diagnoses

Diabetes mellitus.
Hypertensive heart disease.
Cardiac decompensation.
Cerebral hemorrhage.
Intercapillary glomerulosclerosis.

Anatomical Diagnoses

Cerebral thrombosis, left internal carotid artery.
Cerebral infarction, left parietal lobe.
Intercapillary glomerulosclerosis.
Cardiac hypertrophy, hypertensive type.
(Diabetes mellitus.)
Arteriosclerosis, generalized, severe.

Pathological Discussion

Dr. Benjamin Castleman: At autopsy, this patient showed a thrombosis of the left internal carotid, with an infarct of the left parietal lobe. The heart was hypertrophied, weighing a little over 500 gm. The hypertrophy was for the most part left ventricular, characteristic of the hypertensive type. The kidneys were large, smooth surfaced and somewhat swollen, and at the time of autopsy a definite gross diagnosis could not be made. Microscopically, however, there is no doubt that this is the type of sclerosis within the glomerular tufts that was first described in 1936 by Kimmelstiel and Wilson,[1] the type associated with hypertension, diabetes and very often edema. Practically every tuft shows sclerosis and hyalinization of the connective tissue between the glomerular capillaries. The hyalinization occurs in the central portions of the glomeruli, leaving the peripheral capillaries open.

Dr. Talbott: Are these cases all associated with diabetes?

Dr. Castleman: I believe so. Recently, the clinical features of this syndrome have been more fully described by Derow and his associates[2] and by Newburger and Peters.[3]

References

1. Kimmelstiel, P., and Wilson, C. Intercapillary lesions in the glomeruli of the kidney. *Am. J. Path.* 12:83-97, 1936.
2. Derow, H. A., Altschule, M. D., and Schlesinger, M. J. The syndrome of diabetes mellitus, hypertension and nephrosis. *New Eng. J. Med.* 221:1012-1015, 1939.
3. Newburger, R. A., and Peters, J. P. Intercapillary glomerulosclerosis: a syndrome of diabetes, hypertension and albuminuria. *Arch. Int. Med.* 64:1252-1264, 1939.

CASE 27382

Presentation of Case

First Admission. A fifty-year-old man was admitted to the Medical Service complaining of cough with occasional blood-streaked sputum.

The patient was apparently in good health until seven years before admission, when he developed a severe cold, which confined him to bed for five days and to his home for one week longer. The cold was associated with a severe distressing cough, which caused him to raise occasional blood-streaked sputum. At times, he stated that he had coughed clots of dark-red blood. Following paroxysms of coughing, he occasionally vomited. Fol-

lowing this illness, he noted a persistent wheeze with respiration and a rather constant easy fatigability, malaise and general torpor. During the following six years before admission, he suffered frequent colds, usually in the "chest," which occurred mostly in the winter. With these colds, he experienced difficulty in breathing; he was required to sleep on at least two pillows because lying flat seemed to suffocate him. During this six-year interval, he had also what he described as chronic indigestion and the presence of a vague pain, sometimes sharp, usually associated with coughing and located in the region between the shoulder blades.

Physical examination revealed a thin, wasted, ill-developed man who coughed frequently. There was an acneform eruption over the back. The teeth were dirty and carious; the chest was slightly asymmetric, and the upper half of the right chest appeared distinctly smaller than the left. There was a slight degree of lateral curvature of the spine. The breathing was described as "rough," and was somewhat prolonged in the expiratory phase. There were coarse musical rales throughout, and a few crepitant rales were audible at the right apex. The diaphragms descended moderately. The right external inguinal ring was slightly dilated. Rectal examination revealed the presence of hemorrhoids.

The temperature, pulse and respirations were normal.

Examination of the urine was negative. Examination of the blood showed a red-cell count of 4,600,000 with 80 per cent hemoglobin, and a white-cell count of 8600 with 75 per cent polymorphonuclears, 17 lymphocytes, 7 monocytes and 1 eosinophil. The smears were negative. The sputum was negative for acid-fast organisms. The stools were guaiac negative. The blood Wassermann reaction was negative. X-ray examination of the chest revealed that the upper part of the right lung field was less radiant than the left. There was a rather dense shadow at the extreme apex. The hilus shadows were increased in size and density on both sides. The larger lung markings were prominent. Both apices were retracted. The patient remained in the hospital for eleven days and throughout the interval ran a temperature that ranged from 98 to 99°F., pulse from 65 to 85 and respirations from 20 to 24. He was discharged to a convalescent hospital for chronic supportive care.

Final Admission (twelve years later). Since the patient's discharge, he had been in many hospitals for treatment of his chest troubles. He ceased work two years before admission "because of his heart." One year before entry, he suffered an attack of pneumonia and had been chronically ill since. One month before entry, edema of the ankles appeared, and the dyspnea became severer. It was stated that he was partially digitalized elsewhere at this time. The evening before admission, the patient suddenly became much worse; he noted extreme dyspnea, with coughing, weakness and great malaise. He was referred to this hospital by a local physician.

Physical examination revealed an emaciated man propped up on the shock table and barely able to respond. He was dyspneic, cyanotic and acutely ill, so that the examination was necessarily cursory and brief. The chest was deformed. The respiratory excursions were small and asymmetric. The heart was enlarged, 10.5 cm. to the left of the mid-sternal line at the fifth intercostal space. The right border of dullness was located 2.5 cm. to the right of the mid-sternal line. There was a loud blowing systolic murmur at the apex. The heart sounds were of fair quality. The radial and brachial arteries were moderately thickened, and there was a questionable slight engorgement of the neck veins. The abdomen was slightly distended, and a fluid wave was present. The dependent portions of the abdomen were dull to percussion. There was mild pitting edema of the ankles and sacrum. The scrotum was large.

The temperature was 100°F., the pulse 80, and the respirations 30.

Examination of the blood showed a red-cell count of 4,800,000 with 90 per cent hemoglobin, and a white-cell count of 28,000 with 82 per cent polymorphonuclears.

On admission, the patient was in extremis. He was dyspneic and semicomatose. He was given morphine sulfate, and a few minutes later the respirations fell to between 7 and 10 per minute. Coramine was given (2 cc. intravenously), and the patient responded by talking and joking with his children.

X-ray examination of the chest at this time revealed the heart to be enlarged, without characteristic configuration. There was haziness in the right lower-lung field, with questionably dilated bronchi in this area. Several minute areas of marked, increased density scattered through the right mid-lung field had the appearance of old lipiodol. The patient was rushed to the ward, and slumped back into a nearly apneic state, with respirations again 7 to 10 per minute. He was placed in an oxygen tent, and given coramine subcutaneously every four hours, and digalen sub-

cutaneously every two hours for three doses. He lapsed into unconsciousness, and died about sixteen hours after admission.

Differential Diagnosis

Dr. F. Dennette Adams: The evidence provided by the history at the time of the first admission points toward chronic bronchopulmonary infection — tuberculous or nonspecific. The acute illness that ushered in the trouble may have been pneumonia — the duration of the attack, the severe cough and the bloody sputum are most suggestive. Nonspecific bronchopulmonary infection with bronchiectasis, I believe, can develop after pneumonia or certain other forms of acute respiratory disease. In the presence of this chronic ailment, recurrent episodes of acute bronchopulmonary infection are common, especially during the winter. Fever, cough and respiratory distress, often with the asthmatic form of breathing, characterize such attacks; between them, cough with purulent sputum, occasionally bloody sputum and, perhaps, wheezing respiration are the rule. Pulmonary tuberculosis, obviously, must also be considered, on the evidence provided by the history. Blood-streaked sputum, chronic cough and wheezing, especially if the last is unilateral, when they appear in middle life or beyond should always put one on the alert for bronchiogenic tumor. In this case, the duration of the illness is long for tumor.

The pain associated with coughing is best explained on the basis of a chronic pleuritis. The chronic indigestion seems to be of no importance so far as diagnosis is concerned.

The contraction of the upper half of the right chest and the crepitant rales at the right apex found on physical examination point toward chronic tuberculosis; so does the fact that the man had obviously lost weight. The musical rales, however, are more suggestive of chronic bronchitis or asthma. Nothing in the picture as a whole, however, points toward bronchial asthma as the underlying disturbance.

Failure to find tubercle bacilli in the sputum is of some significance, yet it by no means excludes active tuberculosis. It is rather surprising that the discharge diagnosis did not include at least a question of pulmonary tuberculosis, for there were low-grade fever, even with the patient in bed, bloody sputum, and clinical and roentgenologic evidence of disease at the apices.

With everything taken into consideration, I do not believe a definite diagnosis could have been established at the time of discharge from the first hospital admission.

Twelve years later, nineteen years after the trouble began, an acute episode starting less than a day earlier brought the patient back to the hospital. His symptoms of bronchopulmonary disease had continued, and he had also developed symptoms that were thought to have been related to his heart. More recently, increasing dyspnea and edema of the ankles had appeared.

On physical examination, dyspnea, cyanosis, enlargement of the heart, slight engorgement of the neck veins, ascites and dependent edema were noted — all indicative of right-sided heart failure. The patient also had slight elevation of temperature, definite elevation of respiratory rate and an elevated leukocyte count.

The roentgenologist reported cardiac enlargement and changes in the right lower-lung field. Nothing is stated about the changes previously noted in the upper-lung fields, but it is fair to assume that they were still present. Perhaps only additional changes, compared to those seen in the previous plate, were reported.

We have, then, a man first taken sick with a bronchopulmonary disturbance at the age of fifty, remaining chronically ill with respiratory-tract troubles for nineteen years, and eventually dying of what appears to be right-sided heart failure, with perhaps a terminal acute pulmonary infection. The last named is suggested by the fever and elevated leukocyte count. In my opinion, the problem can be reduced to that of deciding whether the underlying disturbance was tuberculous or nontuberculous. Despite the bloody sputum, the harassing cough and the wheezing, tumor can be excluded by the long course of the disease and the roentgenologic findings. A patient with a bronchiogenic tumor could hardly live this long and still have the diagnosis in doubt. The duration of the illness, the cough, bloody sputum and x-ray findings are consistent with tuberculosis. Yet they are just as consistent with nonspecific bronchopulmonary infection and bronchiectasis. Furthermore, the recurrent attacks of acute infection and the apparent development of right-sided heart failure are strong evidence in favor of the nontuberculous type of disease. It hardly seems likely to me that in the presence of active tuberculosis, the patient could have had so many acute episodes and still recover from them. With tuberculosis of sufficient severity to make him as sick as he was, one of the acute attacks might well have been even more serious or prolonged and resulted in earlier death, or at least after nineteen years one would expect a more characteristic clinical picture of chronic active tuberculosis. Furthermore, in tuberculosis of this duration, x-ray findings should be conclusive.

Taking all these factors into consideration, I am led to the conclusion that the patient died of chronic, nonspecific bronchopulmonary infection, bronchiectasis and cor pulmonale, with right ventricular failure. Acute bronchopneumonia was probably a terminal event. Healed tuberculosis of the apices is likely; the x-ray findings in the upper-lung fields cannot be disregarded.

A Physician: Could this possibly be a cerebral embolus to explain the sudden death on this same basis?

Dr. Adams: Cerebral embolus usually originates in the left auricle in cases of mitral stenosis with or without auricular fibrillation, in chronic auricular fibrillation from other causes, in the left ventricle in cases of coronary occlusion with left ventricular infarction, and in subacute bacterial endocarditis, involving the mitral or aortic valve. None of these were present in this case, nor were there any signs of a cerebral vascular accident.

A Physician: Why do you rule out tuberculosis in your diagnosis?

Dr. Adams: The course of the disease is not typical of tuberculosis, and at the end of nineteen years, changes in the lung more characteristic of progressive tuberculosis should be demonstrable roentgenologically.

Clinical Diagnoses

Bronchiectasis, with pneumonitis.
Old pulmonary tuberculosis.
Congestive heart failure.
Cor pulmonale?

Dr. Adams's Diagnoses

Chronic nonspecific bronchopulmonary infection.
Bronchiectasis.
Cor pulmonale.
Right ventricular failure.
Terminal acute bronchopneumonia.
Healed apical tuberculosis?

Anatomical Diagnoses

Pulmonary emphysema.
Pulmonary fibrosis, bilateral.
Bronchiectasis.
Bronchopneumonia, right lower lobe.
Septicemia, *Staphylococcus aureus*.
Cor pulmonale.
Pulmonary tuberculosis, healed apical, bilateral.
Arteriosclerosis, moderate cerebral, coronary and aortic.
Peripheral edema.
Pleuritis, chronic fibrous.
Ascites.

Pathological Discussion

Dr. Tracy B. Mallory: The fundamental process in this case was a chronic, or perhaps more correctly recurrent, pulmonary infection and resultant destruction of the parenchyma of the lungs. At both apices were extensive scars that appeared quite characteristic of healed tuberculosis. There were no foci of activity. Elsewhere, there were extensive fibrosis and emphysema, as well as a diffuse bronchiectasis of many of the smaller radicles of the bronchial tree. It is very improbable that this was due to tuberculosis. There was a terminal acute infection, with spotty foci of early consolidation from which we grew *Staphylococcus aureus*.

The heart was moderately hypertrophied and markedly dilated on the right side, the right auricle being particularly capacious. The right ventricle measured 8 mm. in thickness, which is double the normal value. There can therefore be no doubt of the diagnosis of cor pulmonale. I assume that sudden right-sided heart failure, perhaps precipitated by an infection, was the explanation of the terminal episode. A little qualification is necessary, however, since the coronary arteries showed extensive atheroma, with marked narrowing of their lumens but no points of occlusion. There was enough coronary involvement, however, to make it possible that there was also some left-sided heart failure.

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The Journal does not hold itself responsible for statements made by any contributor.

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AMERICAN ACADEMY OF PEDIATRICS

From October 8 to 11, the American Academy of Pediatrics will hold its eleventh annual meeting in Boston, with general headquarters at the Hotel Statler.

The membership of the academy, which is the largest pediatric society in the world, is made up of licentiates of the American Board of Pediatrics, and consists of 1400 pediatricians in the United States and Canada. The purpose of the organization — to elevate and maintain standards of practice, teaching, research and public health — is achieved through its annual and regional meetings and through its official organ, the *Journal of Pediatrics*. The academy, with the assistance of local committees and in collaboration with state medical societies, supports federal, state and local agencies in child health, initiates such work in communities where the need exists, and prepares manuals containing information on immunization, vitamins and health records.

The American Academy of Pediatrics was one of the first medical groups to present subjects by the so-called "round-table method." This year, the program, as noted elsewhere in this issue of the *Journal*, will consist of round-table conferences on allergy, adolescence, feet and shoes, speech defects, orthodontia, adoption and other subjects. In addition to clinics at three Boston hospitals, there will be panel discussions by eminent authorities on vitamin B, intestinal obstruction, and growth and development. Surgeon General Thomas Parran and others will discuss the role of the pediatrician in national defense.

Owing to the large membership and limited seating facilities, the clinics and round-table conferences will be restricted to members of the academy; members of hospital staffs and public-health boards can be admitted without fee to the panel discussions and the scientific exhibits by presenting proper credentials at the registration desk, where guest badges may be obtained. Detailed information can be obtained from Dr. Lewis W. Hill, 319 Longwood Avenue, Boston, chairman of the Committee on Arrangements.

The Massachusetts Medical Society and the *Journal* extend a cordial welcome to the members of the American Academy of Pediatrics.

THE SCHOOL LUNCH

The Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association, taking cognizance of the importance of the school lunch, has recently released an official statement concerning this increasingly significant unit in the American dietary.

In adapting the school lunch to the needs of the child, one must recognize and correct the principal nutritional deficiencies most commonly found in American diets. These are calcium, vitamin

B_1 and, in certain areas, iron, iodine and the pellagra-preventive factors, nicotinic acid and riboflavin. Where money is actually lacking for the purchase of food, a deficiency in all the essentials may exist.

Further elaboration is found in the section concerning the food sources from which these deficiencies can be made up: milk for calcium, riboflavin and nicotinic acid; eggs for phosphorus and iron; cheese for calcium and phosphorus; vegetables, fruits and meats for many minerals, including iron; whole grains and the legumes for thiamin; and so forth. Practical elementary advice is given concerning the attractiveness of the diet, economic factors and care in preparation.

The proper and safe feeding of a vast multitude of people, whether in a congested city, in an army or in a nation, constitutes an appalling problem. Not only must a suitable diet be furnished, — and an increasing number of newly discovered factors must be considered, — but the difficulties of transportation and preservation and the economic laws of barter and exchange must be observed.

By and large, in this country, few persons need go hungry or badly nourished. A great deal of education in the selection and preparation of food is necessary, however. We have habituated ourselves to absorbing our calories on the move or at the counter without any loss of time, and with little regard to the balanced diet. A few years ago, at Harvard University, historic, impressive Memorial Hall was forced to close its kitchens and the infinite perspective of its great dining room: the students, too impatient to sit, preferred to champ their hamburger rolls with one foot on a rail. If we do not mend our ways and find again the repose that comes from dining, even the Johnsonian* era will come to an end, replaced by curb service — if the gasoline holds out!

*Howard.

MEDICAL EPONYM

Karell Diet

Philip J. Karell (1806–1886), physician to His Majesty, the Emperor of Russia, read a paper, "On the Milk Cure," before the Medical Society of St. Petersburg on March 8 and 23, 1865. This was first printed in the *St. Petersburger medizinische Zeitschrift* (**8:** 193–220, 1865). A translation from the author's manuscript by Dr. G. L. Carrick appears in the *Edinburgh Medical Journal* (**12,** Pt. 1: 97–122, 1866), and the essay in *Archives générales de médecine* (**8:** 513–533, 694–704, 1866). A portion of the translation follows:

> . . . . After a great deal of experience, I have arrived at the conclusion, that in *all dropsies*, in *asthma*, when the result of emphysema and pulmonary catarrh, in obstinate *neuralgia*, when its cause lies in the intestinal canal, in diseases of *the liver* (simple hypertrophy and fatty degeneration), and generally in diseases where there is faulty nutrition . . . milk is the best and surest of remedies. . . .
>
> . . . . I generally commence the cure by employing milk *alone*, and forbidding all *other kinds of nourishment*. I proceed with great caution in prescribing for the patient, three or four times daily, and at *regularly-observed intervals*, half a tumbler or a tumbler, *i.e.*, from 2 to 6 ounces, of skimmed milk. . . . During the second week two ordinary quarts are generally administered each day.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

Albuminuria, Followed by Fatal Sepsis

A thirty-one-year-old primipara was sent into the hospital about three weeks before the expected date of confinement because of albuminuria and a systolic blood pressure of 160.

The care during pregnancy had not been entirely satisfactory. The patient had been seen in the third month but probably not again until the seventh month, when nothing abnormal was noted. In the thirty-sixth week, the blood pressure had risen to 150 systolic, 100 diastolic, and a large trace of albumin had appeared in the urine; a good deal of edema was also present. The next week, the blood pressure was 160 systolic, and the patient was sent into the hospital for induction.

Induction of labor was considered because of the albuminuria and hypertension. Labor was induced by the rupture of the membranes, and after ten hours, twins were delivered. The first baby was delivered by low forceps, and the second by version. Three days after delivery, the temperature rose; at the same time, the patient developed a sore throat. She developed phlebitis, a septic

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section. Letters should be addressed to Dr. Raymond S. Titus, *Secretary*, 330 Dartmouth Street, Boston.

hip, abscess in the back, many pulmonary infarcts and osteomyelitis of the hip. She was transfused twice. Prontylin was given, but not until the one hundred and twenty-first day of hospitalization. The patient died one hundred and forty-four days after delivery, the temperature vacillating all the time from the third day. Permission for an autopsy was not obtained.

Comment. This case represents a type of sepsis that was not infrequently seen years ago. There was no report of blood culture, but such cases are frequently staphylococcal in origin. It is perfectly possible that the infection was induced by the sore throat. It is more probable that the rupture of the membranes and the uterine manipulations of forceps and version were contributory causes. Chemotherapy, applied as it would be today, very early in the onset of this condition might have changed the course of the disease. If the infection had been caused by a streptococcus, it is almost certain that the fatal outcome would have been prevented; if it had been staphylococcal, it is possible that immune transfusions, resorted to early, would have changed the result. Today, any patient who shows signs of infection after delivery should have cultures taken from the throat, blood stream and uterus to determine the specific etiology. After the organism has been identified, intelligent therapy should be instituted immediately. The uterus itself should never be entered. Chemotherapy should be applied in cases in which the organism is one for which the treatment by chemotherapy is known to be valuable. When the infection is staphylococcal, immune transfusions — even though they entail much skilled laboratory work — should be attempted unhesitatingly. All such cases in open wards should be isolated for the protection of other patients. If isolation in puerperal sepsis is not scrupulously followed, epidemics may quickly result. There are about eighty-five deaths each year from puerperal sepsis in Massachusetts. The number should be markedly reduced by the intelligent use of chemotherapy and the intelligent handling of all cases by isolation in maternity hospitals. It must be remembered that even though chemotherapy is invaluable, prevention is more valuable, and that until more adequate supervision is made possible throughout the State, — thereby ensuring clean, gentle operative obstetrics when it is necessary and eliminating much operative obstetrics that would thus be proved unnecessary, — the number of deaths from sepsis will not be materially reduced.

STATED MEETING OF THE COUNCIL

A stated meeting of the Council will be held in John Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Wednesday, October 1, 1941, at 10:30 o'clock.

Business:

1. Presentation of record of meeting held May 21 and 22, 1941, as published in the *New England Journal of Medicine* for June 26, 1941.
2. Reports of standing and special committees.
3. Appointment of an auditing committee.
4. Fill any vacancies in the offices of the Society.
5. Such other business as may lawfully come before this meeting.

MICHAEL A. TIGHE, *Secretary.*

IMPORTANT ADDENDA TO BE CONSIDERED BY THE COUNCIL

The Executive Committee will submit the following resolution. The necessity for this resolution has grown out of the confusion which has arisen in the interpretation of certain phraseology contained in Chapter V, Section 2 of the By-Laws of the Massachusetts Medical Society. The resolution, which seeks to have the Council of the Massachusetts Medical Society interpret this language, is as follows:

Whereas, the Massachusetts Medical Society is desirous that all skillful and ethical practitioners of medicine in Massachusetts shall be members of the Massachusetts Medical Society;

Whereas, Chapter V, Section 2, of the By-Laws of the Massachusetts Medical Society provides the means by which practitioners in medicine in Massachusetts may become members of the Massachusetts Medical Society;

Whereas, by the language involved in Chapter V, Section 2, of the By-Laws of the Massachusetts Medical Society the Council of the Massachusetts Medical Society intends that it shall have accurate knowledge of the training, medical skill and ethical conduct of those who seek admission to membership in the Massachusetts Medical Society;

Whereas, in the case of graduates of nonapproved schools, Chapter V, Section 2, of the By-Laws of the Massachusetts Medical Society provides that the applicant for membership in the Massachusetts Medical Society shall have been in the practice of medicine for a minimum of five years;

Whereas, in establishing such a period of probation for graduates of nonapproved schools, the Council of the Massachusetts Medical Society intends that it shall have had opportunity to closely observe the medical skill and ethical conduct of such applicants;

Whereas, in the case of most graduates of foreign medical schools who have been in the practice of medicine for five years in foreign countries, the Council of the Massachusetts Medical Society has no opportunity to know of the training or adequately observe the medical skill and ethical conduct of such medical practitioners; therefore be it

Resolved, that the Council of the Massachusetts Medical Society interprets the phrase "who has practiced for a minimum of five years," as appearing in the By-Laws of the Massachusetts Medical Society, Chapter V, Section 2 (*b*), to mean what is meant by the phrase, who has lawfully practiced medicine for a minimum of five years in the United States; be it further

Resolved, that the Council of the Massachusetts Medical Society shall be considered to have accurate knowledge of the medical training and medical skill of such graduates of foreign medical schools who have practiced medicine in foreign countries for five years and who are eminent in the profession of medicine and well known to the Council of the Massachusetts Medical Society for their scientific attainments, provided such practitioners shall have satisfied the Council of the Massachusetts Medical Society that their medical practice has been ethical according to the standards as set down in the Code of Ethics of the American Medical Association.

The Executive Committee will recommend to the Council of the Massachusetts Medical Society that the annual meeting of the Council of the Massachusetts Medical Society take place on the evening before the annual meeting of the Society, and that the annual meeting of the Society be moved up from the second day of the annual meeting to the first day.

It is believed that this does not involve any changes in the By-Laws.

If this recommendation is adopted, members of the Council will have an opportunity to attend the scientific exercises throughout these sessions. This opportunity has been seriously curtailed under the present setup.

The following is submitted by the Special Committee Concerned With Prepayment Medical Care Costs Insurance. This matter comes to the Council as a part of the report of and with approval of the Committee on Public Relations; the Executive Committee has considered this presentation at great length and recommends it to the earnest consideration of the Council. It has to do with a tentative set of by-laws to govern a corporation (The Massachusetts Medical Service) proposed to be set up under the permissive legislation passed by the current session of the Massachusetts Legislature.

ARTICLE I

Principal Office and Seal

Section 1. The principal business office of the corporation shall be in the City of Boston, County of Suffolk, Commonwealth of Massachusetts.

Section 2. The seal shall be circular in form, with the words "Massachusetts Medical Service" around the periphery and the words and figures "1941 Massachusetts" within.

ARTICLE II

Membership of the Corporation

Section 1. The members of the corporation shall consist of those persons who shall from time to time be the members of the Executive Committee of the Massachusetts Medical Society.

Section 2. Each member of the corporation shall be entitled to one vote.

Section 3. The annual meeting of the members of the corporation for the choice of directors and the transaction of such other business as shall properly come before the meeting shall be held at the office of the corporation in the City of Boston, or at such other place as may be stated in the call of the meeting, on the last Tuesday of March in each year if not a legal holiday and if a legal holiday then on the next secular day following. In case the annual meeting shall not be duly called and held, the Board of Directors shall call a special meeting in lieu of and for the purpose of such annual meeting and all proceedings at such special meeting shall have the same force and effect as at an annual meeting.

Section 4. Special meetings of the members shall be called by the clerk whenever the Board of Directors or the President shall so order, or upon written request of three or more members, and such request shall state the purpose of such meeting.

Section 5. Notice of the annual meeting and of all special meetings of the members shall be given by the clerk by mailing or delivering to each member at least seven days before the day fixed for the meeting a notice stating the place, day and hour and purpose of the meeting.

Section 6. At every meeting of the members, there shall be represented in person or by proxy at least a majority of the members to constitute a quorum, but a smaller number may adjourn from time to time.

ARTICLE III

Board of Directors

Section 1. The affairs, property and business of the corporation shall be managed by a board of fifteen directors, who may exercise all such powers of the corporation as are not by law or by these by-laws required to be otherwise exercised. Directors need not be members of the corporation.

A majority of the directors shall at all times be persons approved in writing by the Massachusetts Medical Society. One third of the directors shall be physicians registered to practice medicine in the Commonwealth of Massachusetts and engaged in the active practice of medicine in the Commonwealth, and one third shall be persons who are or who agree to become subscribers to the nonprofit medical service plan to be operated by the corporation.

Section 2. The incorporators at their first meeting shall elect five directors to hold office until the first annual meeting, five to hold office until the second annual meeting, and five to hold office until the third annual meeting. At each annual meeting, the members of the corporation shall elect five directors to hold office for a term of three years and thereafter until their successors are elected, provided, however, that at least thirty days before each annual meeting the members shall submit to the President of the Massachusetts Medical Society a list of those persons whom they propose to elect as directors.

Section 3. Any director may be removed from office by a majority of the members of the corporation either by writing filed with the clerk of the corporation or by a vote passed at a meeting of the said members.

Section 4. Vacancies in the Board of Directors occurring during the year shall be filled by a majority vote of those members present at a meeting duly called for such

purpose, provided, however, that at least thirty days prior thereto the members shall submit to the President of the Massachusetts Medical Society the name of the person they propose to elect as a director.

Section 5. A majority of the directors in office for the time being shall constitute a quorum for the transaction of business, but a smaller number may adjourn from time to time.

Section 6. Regular meetings of the directors shall be held immediately after the adjournment of the annual meeting of the members of the corporation at the place of holding the annual meeting and at such times and places as the Board of Directors may determine and no notice of such meetings shall be necessary. Special meetings may be held in like manner and shall be called by the clerk whenever the President or any three directors shall so request in writing, and three days' notice of such meetings shall be given to each director not joining in the request for such meetings unless shorter notice shall be reasonable in the circumstances. Any meeting of the Board of Directors shall be a legal meeting without notice if each director, by a writing filed with the record of the meeting, waives such notice.

Section 7. The Board of Directors shall have power to purchase any property or rights and to enter into any contracts which they deem advantageous to the corporation, to fix the price to be paid by the corporation for such property, rights or contracts, to borrow money, to issue bonds, debentures or other securities of the corporation and pledge or sell the same for such sums and at such prices as they may deem expedient, to adopt rules and regulations subject to the provisions of Article IV hereof and in general to exercise such other powers and to do all such other things as are not required by any other article of the by-laws to be exercised or done by any committee named therein.

No contract or other transaction between this corporation and any other corporation shall in any way be affected or invalidated by the fact that any of the directors of this corporation are pecuniarily or otherwise interested in or are directors of such other corporations and any director of this corporation may be a party to and may be pecuniarily or otherwise interested in any contract or transaction of this corporation provided that the fact that he is so interested shall be disclosed or shall be known to the Board of Directors or a majority thereof and his vote shall not be necessary to authorize or ratify any such contract or transaction.

Section 8. Directors as such shall not receive any stated salary for their services, but by resolution of the board a fixed sum and expenses of attendance, if any, may be allowed for attendance at board meetings. Nothing herein contained shall be construed to preclude a director from serving the corporation in any other capacity and receiving remuneration for such service.

Section 9. The Board of Directors may from time to time delegate any of its powers to committees or officers, attorneys or agents of the corporation subject to such regulations as may be adopted by the board.

ARTICLE IV

Committees

Section 1. The directors may appoint such committees as they deem necessary, including an Administrative Committee and a Finance Committee, and they shall appoint a Central Professional Committee and an Actuarial Research Committee as provided herein.

Section 2. There shall be a Central Professional Service Committee composed of five directors appointed by the president of the corporation, of whom four including the chairman shall be physicians registered to practice in the Commonwealth of Massachusetts. The chairman of the Committee shall be designated by the president of the corporation.

Section 3. The Central Professional Service Committee shall have delegated to it control and supervision over the medical aspects of all matters relating to (a) the standards of medical care to be furnished subscribers, (b) the qualifications of specialists, (c) the extent and classification of medical benefits to be furnished subscribers, (d) the determination of income groups eligible to become subscribers, (e) the compensation to be paid participating physicians, and (f) the admission, suspension and discipline of participating physicians. All rules and regulations of the corporation relating to the foregoing shall be initiated by the Central Professional Service Committee, provided, however, that any rule or regulation relating to the determination of income groups eligible to become subscribers shall first be approved by the Council of the Massachusetts Medical Society. Whenever the committee shall initiate any change in a rule or regulation, it shall give at least thirty days' notice thereof to the President of the Massachusetts Medical Society.

Section 4. In the event of a complaint relative to the conduct or services of a participating physician or of any controversy between a participating physician and a subscriber or whenever it has reason to believe that a participating physician has been guilty of a violation of the rules and regulations of the corporation, or unprofessional or unethical conduct or of conduct which is liable to endanger the interests of the corporation or of any of its subscribers, the committee shall refer the matter for investigation to the District Professional Service Committee within whose district the physician concerned has his principal office, which shall investigate the matter and shall then report the result of its investigation to the Central Professional Service Committee. If it appears to the Central Professional Service Committee that there is reasonable cause to believe that the participating physician has been guilty of a violation of the rules and regulations of the corporation, of unprofessional or unethical conduct, or of conduct which is liable to endanger the interests of the corporation or of any of its subscribers, it shall assign a date for a hearing giving the participating physician concerned at least seven days' notice thereof. If after hearing, at which the participating physician shall be given full opportunity to be heard, the said committee shall find the said physician guilty, it shall terminate the agreement between the said physician and the corporation, or it may take any other disciplinary action which is proper and appropriate in the circumstances, having first, however, reported to the President of the Massachusetts Medical Society its findings and having obtained his approval of its proposed action.

Section 5. The Central Professional Service Committee shall report its acts and proceedings to the Board of Directors at such times as the Board of Directors shall require.

Section 6. There shall be an Actuarial Research Committee of at least three directors appointed by the president of the corporation who shall designate one of the members as chairman.

Section 7. The Actuarial Research Committee shall obtain actuarial data as to incidence of demand for medical services and the cost thereof, shall analyze the data ob-

tained and report to the Board of Directors thereon. It shall have the power, subject to the approval of the Board of Directors, to engage such persons to assist in this work as it may deem necessary.

ARTICLE V

Officers

Section 1. The officers of the corporation shall be a president, a treasurer, a clerk and such subordinate officers as the Board of Directors shall from time to time appoint with such powers and duties and for such terms of office as the directors may designate. The president shall be chosen from among the directors of the corporation, but other officers need not be. The directors at their annual meeting in each year shall elect the aforesaid officers, provided, however, that the incorporators at their first meeting shall elect a treasurer and clerk to hold office until the first annual meeting. All of the said officers shall hold their respective offices for one year and thereafter until their successors are elected and qualified, subject, however, to removal at any time by vote of a majority of the Board of Directors, except that the officers appointed at the first meeting of the Board of Directors shall hold office only until the first annual meeting and thereafter until their successors are elected and qualified. Vacancies in any of the said offices shall be filled for the unexpired portion of the term by the Board of Directors. Officers may be paid such salary or compensation as the Board of Directors shall determine.

Section 2. The president shall be the chief executive officer of the corporation. He shall preside at all meetings of the Board of Directors. He shall see that all orders and resolutions of the Board of Directors are complied with.

Section 3. The treasurer shall have charge of the corporation's financial affairs, subject however to the supervision and control of the Board of Directors. He shall have the custody of all money and securities except his own bond, which shall be kept by the president. He shall deposit all money and valuables in the name and to the credit of the corporation in such depositaries as shall be determined by the Board of Directors. He shall disburse the funds of the corporation as ordered by the Board of Directors. He shall keep or cause to be kept the corporation's accounts in suitable books wherein every transaction shall be accurately recorded and shall render to the president and directors at regular meetings of the board or whenever they require it an account of his transactions as treasurer and of the financial condition of the company and shall discharge all other duties properly appertaining to his office or which may be attached thereto by the Board of Directors. He shall give bond for the faithful discharge of his duties in such form and in such sum as the Board of Directors may require.

Section 4. The clerk shall keep the records of all meetings of the members and of the Board of Directors and shall give notice of all meetings required by these by-laws. He shall have the custody of the record books of the corporation and shall perform all duties usually incident to the office of clerk and such other duties as may be from time to time assigned to him by the Board of Directors.

ARTICLE VI

District Committees

Section 1. Each district medical society in the Commonwealth may appoint a District Administrative Unit composed of not more than nine members of whom a majority shall be physicians engaged in active practice within the district and shall designate one of the members of the committee who is a physician as chairman.

Section 2. Each District Administrative Unit shall assist in the operation of the medical service plan and in obtaining subscribers thereto within its district and shall perform such duties as the Board of Directors may prescribe. It shall from time to time make recommendations to the Board of Directors as to any phase of the operation of the medical service plan except one within the jurisdiction of the District Professional Service Committee.

Section 3. Each district medical society may appoint a District Professional Service Committee, composed of at least five physicians engaged in active practice within the district and shall designate one member thereof as chairman.

Section 4. Each District Professional Service Committee shall act in co-operation with and under the supervision of the Central Professional Service Committee. It shall from time to time survey the quality of medical care rendered to subscribers within its district and shall report thereon to the Central Professional Service Committee. It may report to the Central Professional Service Committee on the qualifications of specialists within its district and may compile and from time to time revise, under the supervision of the Central Professional Service Committee, a list of specialists within its district according to the accepted policy of the Massachusetts Medical Society, which may be used for the benefit of subscribers to the medical service plan. It shall make recommendations to the Central Professional Service Committee as to all matters within its jurisdiction.

Section 5. Each District Professional Service Committee shall, whenever any matter relating to the services or conduct of a participating physician or relating to a controversy between a participating physician and a subscriber is called to its attention by complaint or otherwise, fully investigate the matter and report hereon to the Central Professional Service Committee.

ARTICLE VII

Subscribers

Section 1. A resident of the Commonwealth may become an unlimited subscriber to the medical service plan provided that his annual income does not exceed such amount as shall be fixed by the Board of Directors as provided in Article III, Section 7, and provided further that he make application to become a subscriber as one of such a group as the Board of Directors may specify.

Section 2. An unlimited subscriber shall be entitled to receive from a participating physician such medical services as are included in the subscriber's contract with the corporation, subject to whatever rules and regulations may be adopted by the Board of Directors relative thereto.

Section 3. A resident of the Commonwealth may become a limited subscriber to the medical service plan if his annual income exceeds such amount as shall be fixed by the Board of Directors on such terms and conditions as the Board of Directors may by regulations prescribe.

Section 4. A limited subscriber shall be entitled only to such benefits as are provided in his contract with the corporation. The corporation shall have no supervision over the amount to be charged by a participating physician for services to a limited subscriber.

Section 5. Subscribers shall have free choice among participating physicians subject to the provisions of Article

VIII, Section 3 hereof, and to the rules and regulations adopted by the Board of Directors.

Section 6. The Board of Directors shall have power to enter into arrangements and agreements with employers, societies, charitable organizations, and governmental agencies and authorities for the payment of part or all of the cost of medical care furnished to any persons who may be entitled to such care under the rules and regulations adopted by the Board of Directors.

ARTICLE VIII

Participating Physicians

Section 1. Any physician registered to practice in the Commonwealth may become a participating physician on complying with the provisions of these by-laws and the rules and regulations of the corporation.

Section 2. A physician desiring to become a participating physician shall make written application in the form prescribed by the rules and regulations and shall before becoming entitled to act as a participating physician enter into a written agreement with the corporation in the form prescribed by the rules and regulations.

Section 3. A participating physician shall have the right to accept or reject patients so far as subscribers are concerned and the right to discontinue treatment of any subscriber according to the code of ethics of the American Medical Association, provided, however, he shall not have the right to refuse to accept a subscriber as a patient or to continue treatment of a subscriber for the sole reason that he is a subscriber and such refusal shall constitute grounds for the termination by the corporation of its agreement with a participating physician.

Section 4. A participating physician shall not request or accept from anyone whom he knows to be an unlimited subscriber any compensation for such services as such subscriber is entitled to under his contract with the corporation, except such initial service charge, if any, as may be required by the rules and regulations adopted by the Board of Directors.

ARTICLE IX

Amendment of By-Laws

Section 1. These by-laws may be amended or repealed by vote of the majority of the members of the corporation.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JULY, 1941

Diseases	July 1941	July 1940	Five-year Average*
Anterior poliomyelitis	5	3	9
Chicken pox	519	384	380
Diphtheria	9	7	18
Dog bite	1336	1353	1211
Dysentery, bacillary	26	97	25
German measles	116	30	51
Gonorrhea	344	335	426
Lobar pneumonia	155	183	175
Measles	1420	2830	1331
Meningitis, meningococcal	5	0	3
Meningitis, other forms	8	—	—
Mumps	534	358	313
Paratyphoid fever	4	12	10
Scarlet fever	232	196	240
Syphilis	388	424	442
Tuberculosis, pulmonary	224	255	306
Tuberculosis, other forms	31	18	30
Typhoid fever	5	3	15
Undulant fever	4	4	4
Whooping cough	659	521	520

*Based on figures for preceding five years.

Geographical Distribution of Certain Diseases

Anterior poliomyelitis was reported from: New Bedford, 3; Quincy, 2; total, 5.

Diphtheria was reported from: Arlington, 1; Boston, 2; Fall River, 3; Gloucester, 1; Somerville, 1; Taunton, 1; total, 9.

Dysentery, bacillary, was reported from: Arlington, 2; Boston, 1; Salem, 1; Waltham, 9; Worcester, 12; Wrentham, 1; total, 26.

Infectious encephalitis was reported from: Waltham, 1; total, 1.

Meningitis, meningococcal, was reported from: Boston, 1; Camp Edwards, 1; Everett, 1; Milford, 1; Palmer, 1; total, 5.

Meningitis, other forms, was reported from: Arlington, 1; Chicopee, 1; Haverhill, 1; Lawrence, 1; Palmer, 1; Quincy, 1; Springfield, 1; Worcester, 1; total, 8.

Paratyphoid fever was reported from: Beverly, 1; Boston, 1; Haverhill, 1; Saugus, 1; total, 4.

Pellagra was reported from: Boston, 1; Wakefield, 1; total, 2.

Septic sore throat was reported from: Arlington, 1; Boston, 3; Brockton, 1; Easton, 1; Somerville, 1; Waltham, 1; total, 8.

Tetanus was reported from: Quincy, 1; total, 1.

Trachoma was reported from: Boston, 1; New Bedford, 1; total, 2.

Typhoid fever was reported from: Boston, 1; Brookline, 1; Dennis, 1; Haverhill, 1; Middleboro, 1; total, 5.

Undulant fever was reported from: Leominster, 1; Westboro, 1; West Brookfield, 1; Whitman, 1; total, 4.

Chicken pox, German measles, mumps and whooping cough showed the usual seasonal decline but were reported above the five-year averages.

Meningitis, both meningococcal and other forms, continued above normal levels.

Dog bite, bacillary dysentery, measles, scarlet fever and undulant fever were at about the expected prevalence for the season.

Anterior poliomyelitis, diphtheria, gonorrhea, lobar pneumonia, paratyphoid fever, syphilis, pulmonary tuberculosis and typhoid fever were less prevalent than usual.

BOOK REVIEWS

Chest X-Ray Interpretation, with Special Reference to Tuberculosis. By J. Burns Amberson, Jr., M.D. 8°, paper, 48 pp., with 30 illustrations. New York: National Tuberculosis Association, 1941. 25 cents.

This small brochure is a short discussion and a description of the commoner x-ray findings in pulmonary tuberculosis. The author has had many years of experience in both diagnosis and treatment of pulmonary tuberculosis. In addition, because of his many years as a student of tuberculosis, he is well qualified for this work.

The book includes an excellent discussion of the technical aspects of x-ray examinations, as well as an intelligent and judicious consideration of the pathogenesis and evolution of tuberculosis, indications for x-ray examinations of the chest, and roentgenographic appearances and interpretations of tuberculous lesions. With the greater popularity of the x-ray apparatus as the standard part of the internist's and the general practitioner's office equipment, intelligent guidance in this subject is indeed welcome. The busy practitioner will find a good deal of common sense as well as sound scientific material clearly written

and well illustrated. Dr. William C. Cutter in his foreword cautions, however, against too much self-reliance by the internists and points out the necessity of expert radiologic consultation, which is still a factor of the medical service.

The National Tuberculosis Association has previously published many authoritative small volumes on different phases of tuberculosis. This brochure is an excellent addition to this fine series of publications and should be read by all interested in the subject of pulmonary tuberculosis.

Emergency Surgery. By Hamilton Bailey, F.R.C.S. Fourth edition. 8°, cloth, 944 pp., with 930 illustrations. Baltimore: Williams and Wilkins Company, 1940. $15.00.

In reading this book, one is struck by the diversity of material presented, for it includes all phases of emergency surgery in various parts of the body. It is to be remembered that in England specialization is far behind the practice of metropolitan America. Over there, a general surgeon is such in fact and can be summoned to deal with any surgical condition by a fellow practitioner. This book represents the wealth of experience accumulated by the more successful surgeon under such a system.

This is the sort of meaty volume that a general surgeon in the smaller hospital enjoys. It solves many of his practical problems, while introducing a minimum of the theory that only confuses a busy practitioner. But this feature also adds an element of weakness, in that some well-established procedures of recent origin are not considered in detail. The Miller–Abbott tube is described, but its use is not specifically recommended in the treatment of the paralytic ileus that so often accompanies peritonitis. Cecostomy and ileostomy, however, are recommended as useful measures in this condition. In discussing the administration of parenteral fluids over a period of days, the author notes the threat of edema, but he does not counsel the use of distilled water and glucose in proper amounts to offset the positive balance of sodium chloride.

One of the outstanding features of the editorial policy used by the author is the case history. This has been largely abandoned in modern textbooks in which the statistical method is presented. However, the case history defines the specific problem far better than a group of figures, and in this book it is used with good effect.

This volume and the book on war surgery edited by the same author are two works that will be appreciated by all who deal with surgical emergencies.

Age Morphology of Primary Tubercles. By Henry C. Sweany, M.D. 8°, cloth, 265 pp., with 73 illustrations. Springfield, Illinois: Charles C Thomas, 1941. $5.00.

This book describes an interesting and extensive clinicopathological investigation of the primary type of tuberculous infection in man. In his studies, the author found a rather remarkable similarity of structure in tubercles of the same approximate age. He also found a definite sequence of changes in all tubercles with respect to maturation, degeneration, regeneration and metaplasia.

In this interesting and novel study, both from pathologic specimens and from thorough x-ray examinations, he concludes that about 90 per cent of the primary infections in which the calcified residues persist may be given an age rating by pathological methods that are accurate within plus or minus 25 per cent in lesions between six months and twenty years of age. The age determination of the tubercle by pathological methods was followed on many contacts and on many selected cases to determine the potential relation of tuberculosis to attacks of pleurisy and pneumonia and to occupations, such as the nursing of tuberculous patients. In most studies, the results were, according to the author, surprisingly accurate. In life, however, this study was found to have little importance, because he found that only about 20 per cent of such primary tuberculous infections are visualized on the x-ray film. He also noted what most of us were taught previously: any lesion that is large and not well calcified is potentially dangerous. In addition, the soft lesions are dangerous.

In a series of cases that were kept under control, such as those of nurses and hospital attendants, the author traced the tuberculous infection to the period of contact at the hospital or sanatorium and obtained certain constant morphologic changes. Thus, he believes that in such cases the method might be applied in determining the liability as well as the probable source of the infection. In addition, he employed this method with some success in studying the reinfectious type, especially when repeated tuberculous infection had been spaced over a period of years. The book offers very interesting and intriguing material for the pathologist and should stimulate as well as help the research worker in the field of tuberculosis. However, the facts that ante-mortem x-ray films reveal only 20 per cent of primary lesions, of which only part reveal any age changes, and that most of them demonstrate no changes after eight years are rather discouraging to the clinicians.

The volume should make a very valuable addition to the library of men engaged in tuberculosis work.

Help Your Doctor to Help You When You Have Sick Headache or Migraine. Edited by Walter C. Alvarez, editor-in-chief, George Blumer, Logan Clendening, Irving Cutter, Howard W. Haggard, Rudolph Matas, Charles W. Mayo, George R. Minot, John H. Stokes and George H. Whipple. 8°, cloth, 37 pp. New York: Harper and Brothers, 1941. 95 cents.

An editorial board of ten distinguished physicians is sponsoring a series of booklets, each dealing with a common complaint. The authorship of these booklets is anonymous, but internal evidence points to the gastroenterology department of the Mayo Clinic as the probable birthplace of the booklet on migraine. Obviously, the writer is an authority on the subject and presents his points of view clearly and forcefully. The only criticism of the medical treatment of the subject is the almost exclusive emphasis on psychic (emotional) factors, and warnings against "mistreatment of the brain," whatever that means.

Efforts to educate patients to co-operate intelligently with their physicians are laudable. The task of supplementing without supplanting the individualized advice of the patient's physician is not easy, and in this respect the author of the booklet speaks like a professor of medicine, directly advising the patient, and not like a self-effacing, diplomatic assistant to the patient's physician. He disparages the efforts of the physician by repeated examinations to discover contributing causes of the headaches and to correct physical abnormalities, which have no proved influence in all cases of migraine. Apparently, the patient puts himself on an elimination diet and selects a "headache reliever." Only once was the reviewer able to

find specific directions to ask the advice of a doctor. The foreword makes clear the fact that the series of booklets is meant to confirm and supplement the efforts of the patient's physician. In view of the importance of enlisting the support of doctors for these booklets, it is to be hoped that other volumes of the series take more pains to talk through the family physician and not around him.

Other subjects so far published are: gastric or duodenal ulcer; gallstone and disease of the gall bladder; colitis; and food allergy.

A Short History of Psychiatric Achievement, with a Forecast of the Future. By Nolan D. C. Lewis, M.D. 8°, cloth, 276 pp. New York: W. W. Norton and Company, Incorporated, 1941. $3.00.

The Thomas W. Salmon memorial lectures, given by the author at the New York Academy of Medicine, form the basis of this book. The first four lectures review briefly the history of psychiatry from ancient times up to 1900. This is not a meticulous medical history, with exact dates and references, but an interpretation of the ideas expressed by physicians and others through the ages, and an evaluation of their influence on modern psychiatric thought. The last two chapters, of most interest to psychiatrists today, concern the modern ramifications of psychiatric thought and research and the prospects for future achievement. Emphasis is placed on the broad aspect of psychiatry, particularly on studies of the patient as a biologic unit; personality organization from infancy to adult life, heredity, environment and adjustment, the relation between mental disease and physical illness, the important social aspect of mental disorder, the education of the public and the training of psychiatrists and psychiatric nurses are a few of the topics discussed.

The book is a worthwhile contribution in which the psychiatrist will find many provocative ideas. Unfortunately, the historical part of the book is not well integrated into the last two chapters, and one is under the impression that the material in the last chapters might have made one fairly long paper, but that the author was forced into the historical field to cover a series of six lectures. This is indeed unfortunate, and one is left with a sense of undigested material that should have been more thoroughly worked over and considerably condensed.

The Heart in Pregnancy and the Childbearing Age. By Burton E. Hamilton, M.D., and K. Jefferson Thomson, M.D.; with a section by Frederick C. Irving, M.D. 8°, cloth, 402 pp., with 35 figures and 22 tables. Boston: Little, Brown and Company, 1941. $5.00.

Never before has the problem of heart disease in pregnancy been so adequately treated as in this book. It is the happy result of teamwork between a veteran cardiologist and a physiologically minded clinical investigator. They have tilled a field that has been somewhat neglected because not fully claimed by either the obstetricians or the cardiologists. It was not until cardiac clinics presided over by internists came to be established in lying-in hospitals that substantial progress began to be made.

Since the opening of the cardiac clinic at the Boston Lying-in Hospital in 1921, approximately 1000 patients with heart disease have been culled from over 50,000 admissions. Most of these were observed personally by the senior author. From this enormous experience, he has been able to delineate more clearly than has hitherto been possible what the hazards of pregnancy are to the woman with heart disease and how they should be dealt with. The fruits of this experience may be judged by the progressive reduction in maternal mortality in this cardiac clinic from 7.6 per cent in the first 250 cases to 2.4 per cent in the last 250. This improvement has been achieved largely by the application of a few simple rules of common sense and frequent prenatal check-ups.

Perhaps the most novel feature of the book is the evidence indicating that there is a lightening of the burden of pregnancy on the cardiovascular system during the last month. Not only have physiologic studies shown a marked decrease in the cardiac output and blood volume at this period, but it appears clinically that there is, at the same time, a corresponding decrease in the incidence of heart failure. These observations have a significant bearing on the management of heart disease in pregnancy. They mean that the common practice of emptying the uterus as soon as the baby is viable is based on a false premise. It is safer to allow a patient who has reached the sixth month to go to term.

In this book, there is a mine of useful information for the interested practitioner.

Physical Medicine: The employment of physical agents for diagnosis and therapy. By Frank H. Krusen, M.D. 8°, cloth, 846 pp., with 351 illustrations. Philadelphia: W. B. Saunders Company, 1941. $10.00.

This book represents a great store of knowledge relative to the underlying principles and practical application of physical medicine or physical therapy. The author has drawn on his personal experience prior to and since he assumed charge of this work at the Mayo Clinic. In addition to this, he has made an exhaustive study of the literature on the subject. There is a listing of over eleven hundred references, three hundred and seventy-four of these being employed to supplement the chapter on light therapy alone. After an introduction, each physical agent is considered, in the following order: physics, source, physiologic effects, technic of application, indications and contraindications. Controversial topics are treated with fairness to both sides. In such cases, the author's preference is not always stressed and often is not even expressed.

From the pedagogical standpoint, the reviewer questions the wisdom of omitting diagrams of a wet cell, the process of ionization or iontophoresis and the structure of the atom, and believes that an adequate presentation of Ohm's law and a more generous discussion of the fundamentals of electrophysics, including the electron theory of matter, should appear in the beginning of the text. The grouping of ultraviolet and infrared rays in the same chapter and the zigzagging or oscillating from one to the other are somewhat confusing, since the former produces definite chemical reactions and the latter is only thermogenetic in character. These two physical measures differ greatly in their indications, contraindications, technics of application and the apparatus from which they are obtained, and hence would seem to require separate consideration.

These flaws, however, are not of sufficient importance to detract greatly from the merits of the book. The author deserves credit for crowding into one volume the essence of physical therapy as it is understood and practiced by the most competent men in this field. The book deserves a place in the library of everyone who is practicing physical therapy, including the specialist in this branch of medicine.

NOTICES

ANNOUNCEMENTS

DR. DAVID AYMAN announces the removal of his office from 371 Commonwealth Avenue to 520 Beacon Street, Boston.

AMERICAN ACADEMY OF PEDIATRICS

The eleventh annual meeting of the American Academy of Pediatrics will be held in Boston from October 8 to 11, with general headquarters at the Hotel Statler. Sessions will be in the form of round-table conferences and panel discussions, and hospital clinics will be held each morning from 10 to 12 and each afternoon from 3 to 5 at the Massachusetts General, Children's and Boston Floating hospitals. There will be a banquet and entertainment on Friday, October 10, at 8 p.m. A fee of $4.00 will be charged for attendance at the dinner and entertainment on Friday evening, October 10.

PENTUCKET ASSOCIATION OF PHYSICIANS

The list of speakers and their subjects that have been scheduled for the 1941–1942 meetings of the Pentucket Association of Physicians is as follows:

October 9 — Physiotherapy: Its use and limitations in general practice. Dr. John G. Kuhns.
November 13 — Thrombosis and Embolism. Dr. John B. Sears.
December 11 — Puerperal Sepsis. Dr. Joseph P. Cohen.
January 9 — Lame Backs. Dr. Frank R. Ober.
February 12 — Treatment of Cardiac Arrhythmias. Dr. Hermann L. Blumgart.
March 12 — Some Diseases of the Nervous System in Children. Dr. Bronson Crothers.
April 9 — Comments on Some Communicable Diseases. Dr. Conrad Wesselhoeft.
May 14 — Convalescent Care of Fractures. Dr. Gilbert E. Haggart.

ASSOCIATION OF MILITARY SURGEONS

A meeting of the Association of Military Surgeons of the United States will be held at the Hotel Brown, Louisville, Kentucky, from October 29 to November 1. All members of the medical profession are cordially invited to attend. The session will conclude with a mass review of military medicine and inspection of Fort Knox.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The next written examination and review of case histories (Part I) for Group B candidates will be held in various cities of the United States and Canada on Saturday, January 3, 1942, at 2:00 p.m. Candidates who successfully complete the Part I examinations proceed automatically to the Part II examinations held in June. Applications for admission to Group B, Part I, examinations must be on file in the Secretary's office not later than October 1, 1941. Applications for Group A must be in the Secretary's office by March 1, 1942. Applications for re-examination in Part I (written paper and submission of case histories) must be on file not later than November 15, 1941. Candidates who are required to take re-examinations must do so before the expiration of three years from the date of their original examination.

The general oral and pathological examinations (Part II) for all candidates (Groups A and B) will be conducted by the entire Board, meeting at Atlantic City, New Jersey, immediately prior to the 1942 meeting of the American Medical Association.

As previously announced in the Board booklet, this fiscal year (1941–1942) of the Board marks the close of the two groups of classification of applicants for examination. Thereafter, the Board will have only one classification of candidates, and all will be required to take the Part I examinations. For further information and application blanks, address Dr. Paul Titus, secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

AMERICAN CONFERENCE ON INDUSTRIAL HEALTH

Industrial physicians and manufacturers from all over the country will attend the second annual meeting of the American Conference on Industrial Health on November 5 and 6, at Chicago Towers in Chicago. The conference will be sponsored by the American Association of Industrial Physicians and Surgeons, which maintains a public forum for all who are interested in the prevention of disease, injury and disability in industry, and in the active supervision and promotion of health in industrial groups.

The opening session, which will be held in the morning, will consist of a symposium on the technical problems of industrial health; this will be conducted from the standpoint of the adjustment of the working environment to the employees and vice versa. The afternoon session will consider the economics of industrial health, including the organization and cost of a health service, and the value of an industrial health service to the employer, the employee and the public.

The morning of the second day will be devoted to a symposium on the social implications of industrial health, including such topics as the extent of an industrial health service, the practical relation of hospital and medical care to industrial health, the part played by legislation, the evaluation of labor turnover, the lack of trained men, the experiences of management and the interests of insurance carriers in the medical and social problems presented.

The sessions will close with a schedule of plant-medical-department inspection, by special arrangement with local industries.

VAN METER PRIZE AWARD

The American Association for the Study of Goiter again offers the Van Meter Prize Award of three hundred dollars and two honorable mentions for the best essays submitted concerning original work on problems related to the thyroid gland. The award will be made at the annual meeting of the association, which will be held at Atlanta, Georgia, on June 1, 2, and 3, provided that essays of sufficient merit are presented in competition.

The competing essays may cover either clinical or research investigations, should not exceed three thousand words in length, and must be presented in English; a typewritten, double-spaced copy should be sent to the corresponding secretary, Dr. T. C. Davison, 478 Peachtree Street, Atlanta, Georgia, not later than April 1.

A place will be reserved on the program of the annual meeting for presentation of the prize essay by the author, if it is possible for him to attend. The essay will be published in the annual *Proceedings* of the association. This will not prevent its further publication, however, in any journal selected by the author.

UNITED STATES NAVAL HOSPITAL

The dates, subjects, and speakers for the 1941–1942 medical meetings at the United States Naval Hospital in Chelsea are listed below. The meetings are scheduled to begin at 8:15 p.m., and are open to those who are interested.

October 10 — The Nature and Treatment of Organic Arterial Disease. Dr. Edward Edwards.
November 14 — The Modern Treatment of Pneumonia. Dr. Maxwell Finland.
December 1 — The Management of Hand Injuries and Infections. Dr. Henry Marble.
January 9 — Blood Transfusions. Dr. Francis T. Hunter.
February 13 — Head Injuries. Dr. Donald Munro.
March 13 — Evaluation of Surgical Risk from a Cardiovascular Viewpoint. Dr. Samuel A. Levine.
April 10 — The Relation between Renal Infection and Hypertension. Dr. Soma Weiss.

SEVENTH POSTGRADUATE SEMINAR IN NEUROPSYCHIATRY

The Metropolitan State Hospital, Waltham, recently announced the opening of the Seventh Postgraduate Seminar in Neuropsychiatry.

The course consists of three units: military neuropsychiatry, October 3 to 31; general psychiatry, November 3 to December 12; and general neurology, January 5 to April 10. It is open to a limited number of graduate physicians. The teaching staff comprises a number of recognized specialists in this field throughout the state, and is under the direction of Dr. Roy D. Halloran, superintendent, Metropolitan State Hospital, and Dr. Paul I. Yakovlev, clinical director, Walter E. Fernald State School.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, September 21

Tuesday, September 23

8 p.m. Massachusetts Society of X-Ray Technicians. Massachusetts Memorial Hospitals.

Wednesday, September 24

*12 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

September 23–May 26. Massachusetts Society of X-Ray Technicians, Inc. Page xii, issue of September 11.

October 8–11. American Academy of Pediatrics, Boston. Page 473.

October 9–May 14. Pentucket Association of Physicians. Page 473.

October 10–April 10. United States Naval Hospital, Chelsea. Notice above.

October 13–24. 1941 Graduate Fortnight of the New York Academy of Medicine. Page 834, issue of May 8.

October 14–17. American Public Health Association. Page 579, issue of March 27.

October 19–23. American Academy of Ophthalmology and Otolaryngology. Page 350, issue of August 28.

October 29–30. New England Postgraduate Assembly. Pages ii–iii, issue of September 11.

October 29–November 1. Association of Military Surgeons. Page 473.

November 3–7 American College of Surgeons. Page vii, issue of July 31.

November 5–6. American Conference on Industrial Health. Page 473.

January 3. American Board of Obstetrics and Gynecology. Page 473.

January 10–11. Forum on Allergy. Page 392, issue of September 4.

April 20–24. American College of Physicians. Page 996, issue of June 5.

District Medical Societies

BERKSHIRE

October 30.
April 30.

BRISTOL NORTH

September 18. North Attleboro.
April 16. Taunton.

ESSEX NORTH

September 24. Governor Dummer Academy, South Byfield.
January 7. Haverhill.
May 6. Lawrence.

ESSEX SOUTH

September 24. Governor Dummer Academy, South Byfield (joint meeting with Essex North District).
November 12. Beverly Hospital, Beverly.
December 3. Salem Hospital, Salem.
January 7. Danvers State Hospital, Hathorne.
February 11. Lynn Hospital, Lynn.
March 4. Essex Sanatorium, Middleton.
April 1. Addison Gilbert Hospital, Gloucester.
May 13. Annual meeting (place to be announced).

FRANKLIN

November 11.
January 13.
March 10.
May 12. Annual meeting.
Meetings will be held at the Franklin County Hospital at 11:00 a.m.

HAMPSHIRE

November 5. Veterans Hospital, Leeds, 4:30 and 6:00 p.m.
January 7. Belchertown State Hospital, 1:00 and 4:00 p.m.
March 4. Hotel Northampton, Northampton, 4:30 and 6:30 p.m.
May 6. Hotel Northampton, Northampton, 8:30 p.m.

MIDDLESEX EAST

November 12.
January 28.
March 18.
May 6.
All meetings will be held at 12:15 p.m. at the Bear Hill Golf Club, Stoneham, except that of May 6, which will be held at Woburn at 6:30 p.m.

MIDDLESEX NORTH

October 29.
January 28.
April 29.

NORFOLK SOUTH

October 2.
November 6.
December 4.
January 8.
February 5.
March 5.
April 2.
May 7.
All meetings will be held at 12:00 noon at the Norfolk County Hospital, South Braintree, with the exception of that of February 5, which will be held at the Quincy City Hospital, Quincy.

PLYMOUTH

October 16. Moore Hospital, Brockton.
November 20. Plymouth County Hospital, South Harwich.
January 15. Brockton Hospital, Brockton.
February 19. Jordan Hospital, Plymouth.
March 19. Goddard Hospital, Brockton.
April 16. Bridgewater State Farm, Bridgewater.
May 21. Lakeville Sanatorium, Middleboro.

WORCESTER

October 8. Rutland State Hospital, Rutland.
November 12. Grafton State Hospital, North Grafton.
December 10. Worcester City Hospital, Worcester.
January 14. St. Vincent Hospital, Worcester.
February 11. Worcester State Hospital, Worcester.
March 11. Memorial Hospital, Worcester.
April 8. Hahnemann Hospital, Worcester.
May 13. Annual meeting, Worcester Country Club, Worcester.

WORCESTER NORTH

October 22. State Hospital, East Gardner.
January 28. Leominster Hospital, Leominster.
April 22. Burbank Hospital, Fitchburg.
July 22. Henry Heywood Memorial Hospital, Gardner.